CONTENTS

General, physical, and inorganic

NO.		PAGE
528	The kinetics of the reaction between methyl chloride and lithium iodide in acetone By FARHAT-AZIZ and E. A. MOELWYN-HUGHES	2635
529	The kinetics of the reaction between methyl iodide and potassium cyanide in aqueous solution By B. W. MARSHALL and E. A. MOELWYN-HUGHES	2640
530	The kinetics of certain ionic exchange reactions of the four methyl halides in aqueous solution By R. H. BATHGATE and E. A. MOELWYN-HUGHES	2642
547	Diffusion studies with phosphatide sols By I. L. THOMAS and L. SAUNDERS	2731
552	Magnetic perturbation of singlet–triplet transitions. Part III. Benzene derivatives and heterocyclic compounds By D. F. EVANS	2753
553	The pentacyanohydride complexes of cobalt(I) and rhodium(I) By W. P. GRIFFITH and G. WILKINSON	2757
554	The infrared spectra of alkali salts of complex fluoro-acids By R. D. PEACOCK and D. W. A. SHARP	2762
561	Complex formation between copper and some organic acids, phenols, and phenolic acids occurring in fruit By C. F. TIMBERLAKE	2795
566	Nuclear resonance spectra of sulphoperamidic acid By R. E. RICHARDS and R. W. YORKE	2821
586	Cyclic organic boron compounds. Part IV. *B*-Amino- and *B*-alkoxy-borazoles and their precursors the tris(primary amino)borons and (primary amino)boron alkoxides By D. W. AUBREY and M. F. LAPPERT	2927
587	Metallic complexes of dimethyl-*o*-methylthiophenylarsine. Part II. Complexes of copper, silver, and gold By B. CHISWELL and S. E. LIVINGSTONE	2931
588	Sodium derivatives of dimethylstannane By S. F. A. KETTLE	2936
590	Mechanism of the azide–nitrite reaction. Part I By G. STEDMAN	2943
591	Mechanism of the azide–nitrite reaction. Part II By G. STEDMAN	2949
593	Magnetic studies with copper(II) salts. Part V. Binuclear derivatives of copper(II) formate involving covalent copper-to-copper δ-bonds By R. L. MARTIN and HANNEKE WATERMAN	2960
595	The kinetics of the oxidation of some bipyridyl and phenanthroline complex ions by the peroxydisulphate ion in aqueous solution By D. H. IRVINE	2977
599	Bromamines. Part I. Mono- and di-bromamine By J. K. JOHANNESSON	2998
600	The cleavage of unsymmetrical organolead compounds by silver ions By F. GLOCKLING and D. KINGSTON	3001
NOTES		
617	Nitrogenous chelate complexes of transition metals. Part II. The tervalent gold complexes of 2,2′-bipyridyl By C. M. HARRIS and T. N. LOCKYER	3083

XUM

NO. PAGE

620 The dissociation constant of fluorine
By A. F. TROTMAN-DICKENSON 3088

621 The infrared spectrum of a platinous complex having a bridging ethylenediamine group with the *trans*-configuration: [bisethylenetetrachloro-μ-ethylenediamine-diplatinum(II)]
By D. B. POWELL and N. SHEPPARD 3089

625 Molybdenum(II) benzoate
By E. W. ABEL, APAR SINGH, and G. WILKINSON 3097

626 Iodyl fluoride
By E. E. AYNSLEY and S. SAMPATH 3099

Physical organic

534 Molecular polarisability. The molar Kerr constants of certain derivatives of diphenyl
By J. Y. H. CHAU, (MRS.) C. G. LE FÈVRE, and R. J. W. LE FÈVRE . . . 2666

535 Molecular polarisability. The contributions of the terms θ_1, θ_2, and θ_3 to the Kerr constant of a substance
By (MRS.) C. G. LE FÈVRE and R. J. W. LE FÈVRE 2670

541 Stereoisomerism of addition polymers. Part III. The optical rotatory power of poly[(+)-1 : 3-dimethylbutyl methacrylate] and of copolymers with methyl methacrylate
By C. L. ARCUS and D. W. WEST 2699

545 The synthesis and isomeric rearrangement of 1-phenylallyl chloride
By G. VALKANAS and E. S. WAIGHT 2720

548 Homolytic substitution at a saturated carbon atom. Part I. Products of the gaseous nitration of t-butylbenzene
By H. C. DUFFIN, E. D. HUGHES, and SIR CHRISTOPHER INGOLD . . . 2734

549 Homolytic substitution at a saturated carbon atom. Part II. Products of the photoinduced gaseous chlorination of t-butylbenzene
By J. D. BACKHURST, E. D. HUGHES, and SIR CHRISTOPHER INGOLD . . . 2742

559 Electrometric titration of the sodium salts of deoxyribonucleic acids. Part VII. The reversible dissociation at low temperatures
By A. R. PEACOCKE and B. N. PRESTON 2783

563 Solutions in sulphuric acid. Part XXV. Cryoscopic measurements on some phenols
By R. J. GILLESPIE and J. V. OUBRIDGE 2804

583 Heats of formation and bond energies. Part I. Trisdiethylaminophosphine
By P. A. FOWELL and C. T. MORTIMER 2913

592 Chemical applications of nuclear quadrupole resonance spectroscopy. Part III. The inductive effect of substituents belonging to the first row of the Periodic Table
By E. A. C. LUCKEN 2954

596 The activation of carbon–carbon double bonds by cationic catalysts. Part VIII. Cyclisation of 1 : 1 : 3 : 3-tetraphenylbut-1-ene
By ALWYN G. EVANS and D. PRICE 2982

597 The formation of carbonium ions by the action of metal salts. Part IV. Ionisation of triarylmethyl chlorides by Friedel–Crafts catalysts in acetic acid
By J. L. COTTER and ALWYN G. EVANS 2988

603 Oxidations of organic compounds with quinquevalent vanadium. Part II. The oxidation of ketones
By J. S. LITTLER and WILLIAM A. WATERS 3014

604 The kinetics of diazo-coupling and iodination of glyoxaline and some deutero-glyoxalines
By A. GRIMISON and J. H. RIDD 3019

606 Aromatic reactivity. Part V. Desilylations of trimethylsilyldiphenyls
By F. B. DEANS, C. EABORN, and D. E. WEBSTER 3031

607 Aromatic reactivity. Part VI. Desilylations of α- and β-trimethylsilylnaphthalene
By C. EABORN, Z. LASOCKI, and D. E. WEBSTER 3034

NO. PAGE

608 The reactivities of substituted benzophenones in oxime formation
By J. D. DICKINSON and C. EABORN 3036

611 The formation of hydrocarbon positive ions in strong proton donors
By W. IJ AALBERSBERG, G. J. HOIJTINK, E. L. MACKOR, and W. P. WEIJLAND . 3049

612 Complexes of aromatic hydrocarbons with strong Lewis acids
By W. IJ AALBERSBERG, G. J. HOIJTINK, E. L. MACKOR, and W. P. WEIJLAND . 3055

615 The rotatory dispersion of yohimbine and some derivatives
By J. A. D. JEFFREYS 3077

Organic

531 Effects of γ-radiation. Part I. Polymer formation from sugars, hydroxy-acids, and amino-acids
By S. A. BARKER, P. M. GRANT, M. STACEY, and R. B. WARD 2648

532 Effects of γ-radiation. Part II. Characterisation of the products from glycollic acid
By P. M. GRANT and R. B. WARD 2654

533 Effects of γ-radiation. Part III. Quantitative studies of the products from glycollic acid
By P. M. GRANT and R. B. WARD 2659

536 Chromones and flavones. Part I. Iodination of 5- and 7-hydroxy-2-methylchromone
By M. V. SHAH and SURESH SETHNA 2676

537 West African timbers. Part II. Heartwood constituents of the genus *Pterocarpus*
By A. AKISANYA, C. W. L. BEVAN, and J. HIRST 2679

538 Reaction of some alkyl iodides with periodate
By A. B. FOSTER, M. STACEY, and R. W. STEPHENS 2681

539 The rearrangement of non-enolisable β-diketones. Part I
By N. H. BROMHAM and A. R. PINDER 2688

540 Triazepines. Part I. 1,2,4-Triazacyclohepta-2,5,7-trienes
By (MISS) E. J. ENGELS, M. LAMCHEN, and A. J. WICKEN 2694

542 Ipecacuanha alkaloids. Part III. The stereochemistry at positions 1′ and 10 of emetine
By A. R. BATTERSBY, R. BINKS, and G. C. DAVIDSON 2704

543 Autoxidation of hindered phenols in alkaline media. Part I
By H. R. GERSMANN and A. F. BICKEL 2711

544 The *O*-toluene-*p*-sulphonyl derivatives of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol
By F. H. NEWTH 2717

546 New heteroaromatic compounds. Part III. 2,1-Borazaronaphthalene (1,2-dihydro-1-aza-2-boranaphthalene)
By M. J. S. DEWAR and R. DIETZ 2728

550 The constitution of suint. Part II. Organic acids
By K. R. DEANE and E. V. TRUTER 2746

551 Reaction of thiosulphate ion with tetraethylthiuram disulphide promoted by some metal cations
By B. SAVILLE 2749

555 Some experiments with furans
By D. A. H. TAYLOR 2767

556 Photochemical transformations of tropolones. Part I. Tetra-*O*-methylpurpurogallin
By E. J. FORBES and R. A. RIPLEY 2770

557 Hydride ions in organic reactions. Part I. Dehydrogenation by triphenylmethyl perchlorate
By W. BONTHRONE and D. H. REID 2773

558 The preparation of some 2-amino- and 2-phthalimidobenzophenones
By M. LAMCHEN and A. J. WICKEN 2779

XUM

NO.		PAGE
560	Steroids and Walden inversion. Part XLIII. The bromination of 3 : 5-*cyclo*-steroids By C. W. SHOPPEE, R. W. REES, G. H. R. SUMMERS, and (in part) G. D. PHILLIPS	2786
562	Studies in the synthesis of terpenes. Part IV. The synthesis of (±)-6β-hydroxy-5 : 5 : 9β-trimethyl-*trans*-decal-2-one By T. G. HALSALL, W. J. RODEWALD, and (in part) D. WILLIS	2798
564	Optically active forms of 3′ : 2″-dibromo-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylic acid, and their stability By MALCOLM CRAWFORD, R. A. M. MACKINNON, and V. R. SUPANEKAR	2807
565	The constituents of high-boiling petroleum distillates. Part V. Some condensed thiophen derivatives in a Kuwait oil By W. CARRUTHERS and A. G. DOUGLAS	2813
567	Quinoxaline derivatives. Part VI. Molecular rearrangements of 3,4-dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide 1-oxide, and of nitromalon-bis-*N*-methylanilide By J. W. CLARK-LEWIS and G. F. KATEKAR	2825
568	The constitution of geodoxin, a metabolic product of *Aspergillus terreus* Thom. By C. H. HASSALL and T. C. MCMORRIS	2831
569	Triethylenediphosphine (1 : 4-diphospha*bicyclo*[2 : 2 : 2]octane) By ROY C. HINTON and FREDERICK G. MANN	2835
570	Reactions of pyridyl benzoates with some perbenzoic acids By J. I. G. CADOGAN	2844
571	Stipitatonic acid. A new mould tropolone from *Penicillium stipitatum* Thom. By W. SEGAL	2847
572	Thiadiazoles. Part VIII. 3-Alkyl(or aryl)-5-alkyl(or aryl)amino-1,2,4-thiadiazoles By FREDERICK KURZER and W. TERTIUK	2851
573	Synthesis of some phenyl-cinnolines, -phthalazines, and -quinoxalines By C. M. ATKINSON and C. J. SHARPE	2858
574	Some new mesoionic compounds By ALEXANDER LAWSON and D. H. MILES	2865
575	Effects of γ-radiation. Part IV. The degradation of D-glucose in aqueous solution by γ-irradiation *in vacuo* By P. M. GRANT and R. B. WARD	2871
576	Submicro-methods for the analysis of organic compounds. Part VIII. Factors associated with submicro-titration in glacial acetic acid By R. BELCHER, J. BERGER, and T. S. WEST	2877
577	Submicro-methods for the analysis of organic compounds. Part IX. Titration of organic bases and amine hydrohalides in glacial acetic acid By R. BELCHER, J. BERGER, and T. S. WEST	2882
578	The preparation of some chroman derivatives By R. H. HALL and B. K. HOWE	2886
579	Synthesis of bis-[*p*-di-(2-chloroethyl)aminophenoxy]alkanes By F. BERGEL and E. REINER	2890
580	Chemical studies in the biosynthesis of purine nucleotides. Part III. The synthesis of 5-amino-1-(β-D-ribofuranosyl)glyoxaline-4-carboxyamide and 4-amino-1-(β-D-ribofuranosyl)glyoxaline-5-carboxyamide By J. BADDILEY, J. G. BUCHANAN, F. E. HARDY, and J. STEWART	2893
581	Mechanisms of catalytic hydrogenation. Part I. An examination of the rôle of alkali and of acid By F. J. MCQUILLIN and W. O. ORD	2902
582	B-Nor-5α-cholestane, B-nor-5β-cholestane, and related compounds By G. H. R. SUMMERS	2908
584	Hydrogenation of oximes with platinum metal catalysts By EDITH BREITNER, ELEANOR ROGINSKI, and PAUL N. RYLANDER	2918
585	The biosynthesis of ricinine By HADASSAH TAMIR and DAVID GINSBURG	2921

XUM

NO.		PAGE
589	The reaction of 1-nitromethylcycloheptene with selenium dioxide By Z. Eckstein, A. Sacha, T. Urbański, and (Mrs.) H. Wojnowska-Makaruk .	2941
594	The conversion of carbamoylmethyl thiolsulphates into thio-oxamides; a new variant of the Willgerodt–Kindler reaction By Brian Milligan and J. M. Swan	2969
598	Reduced cyclic compounds. Part VIII. The synthesis of (±)-6-methoxypodocarpa-5,7,13(14)-triene and (±)-abieta-5,7,13(14)-triene By M. F. Ansell and B. Gadsby	2994
601	The chemistry of fungi. Part XXXVI. A revised structure of sclerotiorin By F. M. Dean, J. Staunton, and W. B. Whalley	3004
602	Bisbenzylisoquinolines. Part III. The synthesis of isoquinoline intermediates By M. F. Grundon	3010
605	Polycyclic cinnoline derivatives. Part II. The symmetrical dinaphthopyridazines By R. S. W. Braithwaite and P. F. Holt	3025
609	The phenylation of some diazines By C. M. Atkinson and C. J. Sharpe	3040
610	Synthetical applications of activated metal catalysts. Part VII. The formation of 2,2′-bipyridyl and 2-2′-pyrrolylpyridine from pyridine under the influence of degassed Raney nickel By W. H. F. Sasse	3046
613	Isothiazole: a new mononuclear heterocyclic system By A. Adams and R. Slack	3061
614	Alkali-metal derivatives of sucrose. Part III. The composition of the mono-*O*-methylsucrose prepared from a trisodium derivative By W. A. P. Black, E. T. Dewar, and D. Rutherford	3073

Notes

616	Synthesis of 2,7-bis-*p*-hydroxyphenyl-2,7-dimethyloctane By A. C. Davis and R. F. Hunter	3081
618	Interaction of tetranitromethane with aromatic hydrocarbons By (Miss) Jayanti Nag Chaudhuri and Sadhan Basu	3085
619	Benzylation of 2-phenylbenzimidazoles By N. V. Subba Rao and C. V. Ratnam	3087
622	Lycopodium alkaloids. Part I. Extraction of alkaloids from *Lycopodium fawcettii*, Lloyd and Underwood By R. H. Burnell	3091
623	Syntheses of the four dimethoxy-*N*-methylphthalimides By H. R. Arthur and (Miss) Y. L. Ng	3094
624	Carcinogenic nitrogen compounds. Part XXVII. Benzacridines and related compounds derived from *o*-ethylaniline By N. Ph. Buu-Hoï and P. Jacquignon	3095
627	Some fatty acid esters of α-tocopherol By P. F. G. Praill	3100
628	The synthesis of 9-alkyl- or 9-aryl-9-arsafluorenes or -9-stibiafluorenes By Denys M. Heinekey and Ian T. Millar	3101
629	Thioxan and 2,2′-dihydroxydiethyl disulphide By K. J. M. Andrews and F. N. Woodward	3102

INDEX OF AUTHORS' NAMES

Aalbersberg, W. I., Hoijtink, G. J., Mackor, E. L., and Weijland, W. P., 3049, 3055
Abel, E. W., Singh, A., and Wilkinson, G., 3097
Adams, A., and Slack, R., 3061
Akisanya, A., Bevan, C. W. L., and Hirst, J., 2679
Andrews, K. J. M., and Woodward, F. N., 3102
Ansell, M. F., and Gadsby, B., 2994
Arcus, C. L., and West, D. W., 2699
Arthur, H. R., and Ng, Y. L., 3094
Atkinson, C. M., and Sharpe, C. J., 2858, 3040
Aubrey, D. W., and Lappert, M. F., 2927
Aynsley, E. E., and Sampath, S., 3099
Backhurst, J. D., Hughes, E. D., and Ingold, Sir C., 2742
Baddiley, J., Buchanan, J. G., Hardy, F. E., and Stewart, J., 2893
Barker, S. A., Grant, P. M., Stacey, M., and Ward, R. B., 2648
Basu, S. See Chaudhuri, J. N., 3085
Bathgate, R. H., and Moelwyn-Hughes, E. A., 2642
Battersby, A. R., Binks, R., and Davidson, G. C., 2704
Belcher, R., Berger, J., and West, T. S., 2877, 2882
Bergel, F., and Reiner, E., 2890
Berger, J. See Belcher, R., 2877, 2882
Bevan, C. W. L. See Akisanya, A., 2679
Bickel, A. F. See Gersmann, H. R., 2711
Binks, R. See Battersby, A. R., 2704
Black, W. A. P., Dewar, E. T., and Rutherford, D., 3073
Bonthrone, W., and Reid, D. H., 2773
Braithwaite, R. S. W., and Holt, P. F., 3025
Breitner, E., Roginski, E., and Rylander, P. N., 2918
Bromham, N. H., and Pinder, A. R., 2688
Buchanan, J. G. See Baddiley, J., 2893
Burnell, R. H., 3091
Buu-Hoï, N. Ph., and Jacquignon, P., 3095
Cadogan, J. I. G., 2844
Carruthers, W., and Douglas, A. G., 2813
Chau, J. Y. H., Le Fèvre, C. G., and Le Fèvre, R. J. W., 2666
Chaudhuri, J. N., and Basu, S., 3085
Chiswell, B., and Livingstone, S. E., 2931
Clark-Lewis, J. W., and Katekar, G. F., 2825
Cotter, J. L., and Evans, A. G., 2988
Crawford, M., Mackinnon, R. A. M., and Supanekar, V. R., 2807
Davidson, G. C. See Battersby, A. R., 2704
Davis, A. C., and Hunter, R. F., 3081
Dean, F. M., Staunton, J., and Whalley, W. B., 3004
Deane, K. R., and Truter, E. V., 2746
Deans, F. B., Eaborn, C., and Webster, D. E., 3031
Dewar, E. T. See Black, W. A. P., 3073
Dewar, M. J. S., and Dietz, R., 2728
Dickinson, J. D., and Eaborn, C., 3036
Dietz, R. See Dewar, M. J. S., 2728
Douglas, A. G. See Carruthers, W., 2813
Duffin, H. C., Hughes, E. D., and Ingold, Sir C., 2734
Eaborn, C., Lasocki, Z., and Webster, D. E., 3034
Eaborn, C. See also Deans, F. B., 3031, and Dickinson, J. D., 3036
Eckstein, Z., Sacha, A., Urbański, T., and Wojnowska-Makaruk, H., 2941
Engels, E. J., Lamchen, M., and Wicken, A. J., 2694
Evans, A. G., and Price, D., 2982
Evans, A. G. See also Cotter, J. L., 2988
Evans, D. F., 2753
Farhat-Aziz and Moelwyn-Hughes, E. A., 2635
Forbes, E. J., and Ripley, R. A., 2770
Foster, A. B., Stacey, M., and Stephens, R. W., 2681
Fowell, P. A., and Mortimer, C. T., 2913
Gadsby, B. See Ansell, M. F., 2994
Gersmann, H. R., and Bickel, A. F., 2711
Gillespie, R. J., and Oubridge, J. V., 2804
Ginsburg, D. See Tamir, H., 2921
Glockling, F., and Kingston, D., 3001
Grant, P. M., and Ward, R. B., 2654, 2659, 2871
Grant, P. M. See also Barker, S. A., 2648
Griffith, W. P., and Wilkinson, G., 2757
Grimison, A., and Ridd, J. H., 3019
Grundon, M. F., 3010
Hall, R. H., and Howe, B. K., 2886
Halsall, T. G., Rodewald, W. J., and Willis, D., 2798
Hardy, F. E. See Baddiley, J., 2893
Harris, C. M., and Lockyer, T. N., 3083
Hassall, C. H., and McMorris, T. C., 2831
Heinekey, D. M., and Millar, I. T., 3101
Hinton, R. C., and Mann, F. G., 2835
Hirst, J. See Akisanya, A., 2679
Hoijtink, G. J. See Aalbersberg, W. I., 3049, 3055
Holt, P. F. See Braithwaite, R. S. W., 3025
Howe, B. K. See Hall, R. H., 2886
Hughes, E. D. See Backhurst, J. D., 2742, and Duffin, H. C., 2734
Hunter, R. F. See Davis, A. C., 3081
Ingold, Sir C. See Backhurst, J. D., 2742, and Duffin, H. C., 2734
Irvine, D. H., 2977
Jacquignon, P. See Buu-Hoï, N. Ph., 3095
Jeffreys, J. A. D., 3077
Johannesson, J. K., 2998
Katekar, G. F. See Clark-Lewis, J. W., 2825
Kettle, S. F. A., 2936
Kingston, D. See Glockling, F., 3001
Kurzer, F., and Tertiuk, W., 2851
Lamchen, M., and Wicken, A. J., 2779
Lamchen, M. See also Engels, E. J., 2694
Lappert, M. F. See Aubrey, D. W., 2927
Lasocki, Z. See Eaborn, C., 3034
Lawson, A., and Miles, D. H., 2865
Le Fèvre, C. G., and Le Fèvre, R. J. W., 2670
Le Fèvre, C. G. See also Chau, T. Y. H., 2666
Le Fèvre, R. J. W. See Chau, J. Y. H., 2666, and and Le Fèvre, C. G., 2670
Littler, J. S., and Waters, W. A., 3014
Livingstone, S. E. See Chiswell, B., 2931
Lockyer, T. N. See Harris, C. M., 3083
Lucken, E. A. C., 2954
Mackinnon, R. A. M. See Crawford, M., 2807
Mackor, E. L. See Aalbersberg, W. I., 3049, 3055
McMorris, T. C. See Hassall, C. H., 2831
McQuillin, F. J., and Ord, W. O., 2902
Mann, F. G. See Hinton, R. C., 2835
Marshall, B. W., and Moelwyn-Hughes, E. A., 2640
Martin, R. L., and Waterman, H., 2960
Miles, D. H. See Lawson, A., 2865

Millar, I. T. See Heinekey, D. M., 3101
Milligan, B., and Swan, J. M., 2969
Moelwyn-Hughes, E. A. See Bathgate, R. H., 2642, Farhat-Aziz, 2635, and Marshall, B. W., 2640
Mortimer, C. T. See Fowell, P. A., 2913
Newth, F. H., 2717
Ng, Y. L. See Arthur, H. R., 3094
Ord, W. O. See McQuillin, F. J., 2902
Oubridge, J. V. See Gillespie, R. J., 2804
Peacock, R. D., and Sharp, D. W. A., 2762
Peacocke, A. R., and Preston, B. N., 2783
Phillips, G. D. See Shoppee, C. W., 2786
Pinder, A. R. See Bromham, N. H., 2688
Powell, D. B., and Sheppard, N., 3089
Praill, P. F. G., 3100
Preston, B. N. See Peacocke, A. R., 2783
Price, D. See Evans, A. G., 2982
Rao, N. V. S., and Ratnam, C. V., 3087
Ratnam, C. V. See Rao, N. V. S., 3087
Rees, R. W. See Shoppee, C. W., 2786
Reid, D. H. See Bonthrone, W., 2773
Reiner, E. See Bergel, F., 2890
Richards, R. E., and Yorke, R. W., 2821
Ridd, J. H. See Grimison, A., 3019
Ripley, R. A. See Forbes, E. J., 2770
Rodewald, W. J. See Halsall, T. G., 2798
Roginski, E. See Breitner, E., 2918
Rutherford, D. See Black, W. A. P., 3073
Rylander, P. N. See Breitner, E., 2918
Sacha, A. See Eckstein, Z., 2941
Sampath, S. See Aynsley, E. E., 3099
Sasse, W. H. F., 3046
Saunders, L. See Thomas, I. L., 2731
Saville, B., 2749
Segal, W., 2847
Sethna, S. See Shah, M. V., 2676
Shah, M. V., and Sethna, S., 2676
Sharp, D. W. A. See Peacock, R. D., 2762
Sharpe, C. J. See Atkinson, C. M., 2858, 3040
Sheppard, N. See Powell, D. B., 3089
Shoppee, C. W., Rees, R. W., Summers, G. H. R., and Phillips, G. D., 2786
Singh, A. See Abel, E. W., 3097
Slack, R. See Adams, A., 3061
Stacey, M. See Barker, S. A., 2648, and Foster, A. B., 2681
Staunton, J. See Dean, F. M., 3004
Stedman, G., 2943, 2949
Stephens, R. W. See Foster, A. B., 2681
Stewart, J. See Baddiley, J., 2893
Summers, G. H. R., 2908
Summers, G. H. R. See also Shoppee, C. W., 2786
Supanekar, V. R. See Crawford, M., 2807
Swan, J. M. See Milligan, B., 2969
Tamir, H., and Ginsburg, D., 2921
Taylor, D. A. H., 2767
Tertiuk, W. See Kurzer, F., 2851
Thomas, I. L., and Saunders, L., 2731
Timberlake, C. F., 2795
Trotman-Dickenson, A. F., 3088
Truter, E. V. See Deane, K. R., 2746
Urbański, T. See Eckstein, Z., 2941
Valkanas, G., and Waight, E. S., 2720
Waight, E. S. See Valkanas, G., 2720
Ward, R. B. See Barker, S. A., 2648, and Grant, P. M., 2654, 2659, 2871
Waterman, H. See Martin, R. L., 2960
Waters, W. A. See Littler, J. S., 3014
Webster, D. E. See Deans, F. B., 3031, and Eaborn, C., 3034
Weijland, W. P. See Aalbersberg, W. I., 3049, 3055
West, D. W. See Arcus, C. L., 2699
West, T. S. See Belcher, R., 2877, 2882
Whalley, W. B. See Dean, F. M., 3004
Wicken, A. J. See Engels, E. J., 2694, and Lamchen, M., 2779
Wilkinson, G. See Abel, E. W., 3097, and Griffith, W. P., 2757
Willis, D. See Halsall, T. G., 2798
Wojnowska-Makaruk, H. See Eckstein, Z., 2941
Woodward, F. N. See Andrews, K. J. M., 3102
Yorke, R. W. See Richards, R. E., 2821

XUM

PAPERS ACCEPTED

Internuclear cyclisation. Part XV. The catalytic decomposition of diazonium chlorides prepared from *ortho*-substituted 2-amino-*N*-methylbenzanilides. By D. H. Hey and R. A. J. Long

The structures of dicyclopentadienyl-tin and -lead. By L. D. Dave, D. F. Evans, and G. Wilkinson

Ultraviolet and infrared spectra of some aromatic nitro-compounds. By C. P. Conduit

Ipecacuanha alkaloids. Part IV. The relative and absolute stereochemistry of the benzoquinolizidine system of emetine. By A. R. Battersby and S. Garratt (née Cox)

The stability constants of some metal chelates of *o*-aminophenols. By P. Sims

A novel reaction of the pyridine ring. By G. E. Ficken and J. D. Kendall

The crystallography of some cyanine dyes. Part II. The molecular and crystal structure of the ethanol solvate of 3,3′-diethylthiacarbocyanine bromide. By P. J. Wheatley

2,3:6,7-Dibenzodiphenylene. By R. F. Curtis

Complex fluorides. Part XII. The structures of some complex acid fluorides. By M. F. A. Dove

The oxygen groups of cassaic acid. By V. P. Arya and D. W. Mathieson

6-Hydroxy-4,5-benzindane. By D. W. Mathieson and V. S. Gandhi

The structures of potassium trifluorocuprate(II) and potassium trifluorochromate(II). By A. J. Edwards and R. D. Peacock

Nitration of *m*-iodonitrobenzene. By R. S. Kapil

Intermediates in arylalkyl systems. Part II. Kinetics and mechanism of substitution of diphenylmethyl bromide by anionic reagents in nitromethane. By Y. Pocker

Intermediates in arylalkyl systems. Part III. Kinetics and mechanisms of substitutions of diphenylmethyl bromide by amines in nitromethane. By Y. Pocker

Experiments relating to phthiocerol. Part IV. Synthesis of 7-methoxy-6-methylnonanoic acid. By F. K. Drayson and N. Polgar

An examination of the Rutaceae of Hong Kong. Part IV. The synthesis of dihydronitidine. By H. R. Arthur and Y. L. Ng

The preparation of 2-nitroacetophenone from *o*-nitroaniline, and the synthesis of 2-phthalimidoacetophenone. By J. M. Bruce and R. I. Fryer

Polyfluoroarenes. Part II. The ionisation constant of pentafluorophenol. By J. M. Birchall and R. N. Haszeldine

Synthetic studies of terpenoids. Part III. By J. R. Mahajan and P. C. Dutta

Diphosphine dioxides. Part I. Some representatives of diphosphine dioxides with a tetra-, penta-, and hexa-methylene bridge. By G. M. Kosolapoff and R. F. Struck

Synthetic studies of terpenoids. Part IV. By S. Mukherjee and P. C. Dutta

The effect of viscosity on the fluorescence yield of solutions. By E. J. Bowen and S. F. A. Miskin

An ester of "phosphoenol-fluoropyruvic acid" [1-alkoxycarbonyl-2-fluorovinyl dialkyl phosphate] and related compounds. By E. D. Bergmann and I. Shahak

The relation between the heat and volume of mixing. By J. S. Rowlinson and A. R. Mathieson

Determination of the ionization constant of hydrocyanic acid at 25° by a spectrophotometric indicator method. By K. P. Ang

Bisquaternary ammonium salts. Part IV. 3-Alkylbenzene-1 : ω-bistrimethylammonium salts. By J. N. Ashley and S. S. Berg

The stretching frequencies of metal–oxygen double bonds. By C. G. Barraclough, J. Lewis, and R. S. Nyholm

The hydrolysis of D-carboxyethylene phosphate (D-glyceric acid 2,3-cyclic phosphate). By R. F. Webb and A. J. Duke

Reactions of triethyltin chloride with amines. By K. K. Joshi and P. A. H. Wyatt

The structure and properties of certain polycyclic indolo- and quinolino-derivatives. Part XIII. The cyclisation of certain 4-pyridyl- and 4-quinolyl-hydrazones. By F. G. Mann, A. F. Prior, and T. J. Willcox

Chlorine hydrate. By K. W. Allen

The structure of laminarin. Part III. Synthesis of structural oligosaccharides. By S. Peat, W. J. Whelan, and J. M. Evans

XUM

Modified steroid hormones. Part XI. 16α-Methyldeoxycorticosterone acetate. By V. Petrow and D. M. Williamson

Kinetic studies of the oxidation of metal ions by cobalt(III) in solution in aqueous perchloric acid. By D. R. Rosseinsky and W. C. E. Higginson

Modified steroid hormones. Part XII. Some propargyl derivatives. By D. Burn, G. Cooley, V. Petrow, and G. O. Weston

Polarographic reduction of tetraphenylcyclopentadienone in dimethylformamide. By P. H. Given and M. E. Peover

The chemistry of fungi. Part XXXVII. The structure of rubropunctatin. By E. J. Haws, J. S. E. Holker, A. Kelly, A. D. G. Powell, and A. Robertson

The chemical action of ionising radiations in solution. Part XXIII. The action of ^{60}Co-gamma-rays on aqueous solutions of ethanol in the liquid and the frozen state. By J. T. Allan, E. M. Hayon, and J. Weiss

Peroxides of elements other than carbon. Part VI. Peroxides of germanium. By A. G. Davies and C. D. Hall

The thermal isomerization of 1,1-dimethylcyclopropane. By M. C. Flowers and H. M. Frey

Anomalous conduction in phosphoric acid hemihydrate, $2H_3PO_4.H_2O$. By N. N. Greenwood and A. Thompson.

Isotope and crystal-field effects in the vibrational spectrum of potassium tetrafluoroborate. By N. N. Greenwood

Steric effects in di- and tri-arylmethanes. Part I. Electronic absorption spectra of *o*-methyl derivatives of Michler's Hydrol Blue and Crystal Violet: conformational isomers of Crystal Violet. By C. C. Barker, M. H. Bride, and A. Stamp

Amino-acids and peptides. Part XIV. Further studies on the synthesis of aspartyl-peptides. By P. M. Bryant, R. H. Moore, P. J. Pimlott, and G. T. Young

Aromatic reactivity. Part IX. Bromo- and chloro-desilylation in acetic acid. By C. Eaborn and D. E. Webster

The reaction of Wittig reagents with phenyl isocyanate. By S. Trippett and D. M. Walker

Steroidal αβ-epoxy-ketones. Part I. Rearrangement of 4α,5-epoxy-5α-cholestan-3-one and its 4β,5β-isomer by means of the boron trifluoride–ether complex. By D. J. Collins

Elaboration products of podocarpic acid. By R. Hodges and R. A. Raphael

Optical rotatory power and molecular structure. Part I. The synthesis and optical resolution of *As*-spirobis-1,2,3,4-tetrahydroarsinolinium iodide. By F. G. Holliman, F. G. Mann, and D. A. Thornton

The ionisation potential of NH. By R. I. Reed and W. Snedden

A new chromone synthesis. By B. B. Millward

Pyrrolo[2,3-*d*]pyrimidines. By J. Davoll

New intermediates and dyes. Part VII. The influence of the t-butyl group on the properties of azoic dyes. By V. Vassiliadis and A. T. Peters

Organic fluorine compounds. Part XV. Some pyrimidines derived from fluoroacetamidine. By E. D. Bergmann and S. Cohen

Comparative reaction rates in solid and in liquid sulphuric acid–water mixtures. By T. G. Bonner and J. C. Lockhart

Organosilicon compounds. Part XXI. Some compounds containing phosphorus. By A. E. Canavan and C. Eaborn

The reactions of *N*-bromo-acetanilides in chlorobenzene and benzene solutions in the presence of acetic and propionic acid. By S. C. Chan and G. C. Israel

The determination of the primary and secondary dissociation constants of some aliphatic dicarboxylic acids. By R. H. Jones and D. I. Stock

A deuterium isotope effect in the oxidation of cyclohexanol by cerium(IV). By J. S. Littler

Aspects of stereochemistry. Part XIV. Addition of hypobromous acid to Δ^1-steroids. By H. B. Henbest and R. A. L. Wilson

Hydrolysis of isopropylideneglycerol esters of fatty acids. By L. Hartman

The effect of pressure on the ionization of some benzoic acids. By R. J. H. Clark and A. J. Ellis

Stereoselective reaction of keten with 3-chlorobutan-2-one; geometry of the 3-methylpent-3-enoic acids. By R. H. Cornforth

Rapid, simple, and inexpensive preparation of [$^2H_3$]methyl iodide and [$^2H_6$]dimethyl sulphoxide. By F. A. Cotton, J. H. Fassnacht, W. D. Horrocks, jun., and N. A. Nelson

Naturally occurring quinones. Part III. A synthesis of digitolutein. By J. C. Lovie and R. H. Thomson

The hydrogen isotope effect in the bromination of ethyl 2-oxocyclopentanecarboxylate at −19·98°. By J. R. Hulett

XUM

The Skraup test for pyridine-2-carboxylic acids. By R. M. Acheson and G. A. Taylor
Carotenoids and related compounds. Part VIII. Novel syntheses of echinenone and cantha-xanthin. By M. Akhtar and B. C. L. Weedon
The solubilisation of some dibasic fatty acids by lecithin in benzene. By P. H. Elworthy
The measurement of the conductance of electrolytes. By W. S. Metcalf
Peptides. Part IX. Preparation of L-phenylalanine from L-tyrosine. By R. S. Coffey, M. Green, and G. W. Kenner
Reactions of some pyrazole derivatives. By I. L. Finar and K. Utting
Chlorine atom exchange between antimony trichloride and trimethylchlorosilane in benzene and hexane. Part II. Kinetics and mechanism of exchange. By A. F. Reid and R. Mills
Aliphatic Friedel–Crafts reactions. Part II. The acylation of cyclopentane. By N. Jones and H. T. Taylor
The configuration of noradrenaline. By P. Pratesi, A. La Manna, A. Campiglio, and V. Ghislandi
Nucleophilic displacements in organic sulphites. Part VI. Comparison of the alkaline hydrolyses of cyclic and open-chain sulphites. By J. G. Tillett
The alkaloids of *Ormosia dasycarpa* Jacks. By R. T. Clarke and M. F. Grundon
Tautomerism of *N*-heteroaromatic aldoximes. By S. F. Mason
5-Oxo-2-phenyl-1,3-dioxan. By A. A. Marei and R. A. Raphael
Studies in the pyrolysis of organic bromides. Part XIV. The unimolecular decomposition of n-pentyl and n-hexyl bromide. By J. H. S. Green, A. Maccoll, and P. J. Thomas
Non-empirical molecular-orbital calculations on benzene. The scale parameter *z*. By E. T. Stewart
Electronic correlation of molar refraction. By S. R. Palit and G. R. Somayajulu
Reactions of disodium pentacyanoaminoferrate with aromatic amines. Part IV. The preparation and properties of compounds containing the μ-*p*-phenylenediaminebis(pentacyanoferrate) ion. By E. F. G. Herington
Preparation of 1-benzylpiperazine. By J. Cymerman Craig
The effect of pressure on the first dissociation constant of " carbonic acid." By A. J. Ellis
The stereochemistry of B sub-group metals. Part II. The inert pair. By L. E. Orgel
Distribution of molecular weights in some polyesters and polypeptides. By M. T. Pope, T. J. Weakley, and R. J. P. Williams
The kinetics of formation of some polyesters. By M. T. Pope and R. J. P. Williams
Molecular polarisation and molecular interaction. Part VIII. The apparent dipole moments of some derivatives of *N*-methylaniline in benzene and dioxan solutions. J. W. Smith and (Miss) S. H. Walshaw
The chemistry of the *Aristolochia* species. Part IV. The structure of aristolactone. By J. W. Steele, J. B. Stenlake, and W. D. Williams
The spectrum of the coronene crystal. By L. E. Lyons and J. R. Walsh
Phthalocyanine crystal spectra. By L. E. Lyons, J. R. Walsh, and J. W. White
Alkyl and aryl derivatives of transition metals. Part II. Platinum(II) derivatives. By J. Chatt and B. L. Shaw
Liquid-phase photolysis. Part I. Variation of isomer ratios with radical source in the phenylation of isopropylbenzene. Photolytic generation of phenyl radicals. By J. McDonald Blair, D. Bryce-Smith, and B. W. Pengilly
The catalytic hydrogenation of unsaturated hydrocarbons. Part IV. The kinetics of the hydrogenation of acetylene over supported and unsupported iron, cobalt, and copper, and over some nickel–cobalt and nickel–copper alloys. By G. C. Bond and R. S. Mann
Syntheses of 1-phenylfluorene and 1- and 3-phenylphenanthrene. By D. M. W. Anderson, N. Campbell, D. Leaver, and (the late) W. H. Stafford
Studies of dipole moments, and sorption characteristics at the solution–solid interface, of a series of substituted phenols. By B. Erié, E. V. Goode, and D. A. Ibbitson
The periodate oxidation of 2-deoxylglycosides: structure of 1-(2-deoxy-*D*-galactosyl)benzimidazole. By R. J. Ferrier and W. G. Overend
An infrared study of the methylhydroxylamines. By M. Davies and N. A. Spiers
Infrared absorption of heteroaromatic and benzenoid six-membered monocyclic nuclei. Part IX. *ortho*-Disubstituted benzenes. By A. R. Katritzky and R. A. Jones
Infrared absorption of substituents in heteroaromatic systems. Part III. Amino-, methylamino-, and dimethylamino-compounds. By A. R. Katritzky and R. A. Jones
The conductance of solutions in which the solvent molecule is " large." Part IV. Amine picrates in triethyl phosphate. By C. M. French, P. B. Hart, and D. F. Muggleton
Electrophoresis of gold and silver particles. By J. T. Harrison and G. A. H. Elton

Tropolones. Part X. Synthesis and properties of 2,3-benzotropone. By G. L. Buchanan and D. R. Lockhart

The rearrangement of 1,2′-hydrazonaphthalene. By E. R. Ward and B. D. Pearson

Vapour pressures of metal alkoxides. Part III. Hafnium tetra-t-butoxide and -t-pentyl oxide. By D. C. Bradley and J. D. Swanwick

The oxidation of diphenylmethylenecyclobutane. By S. H. Graham and A. J. S. Williams

Muscarufin. Part I. The action of diazotised anthranilic acid on 1,4-benzoquinones. By R. L. Edwards and D. G. Lewis

Muscarufin. Part II. 2-(4-Carboxypenta-1,3-dienyl)-1,4-benzoquinones. By R. L. Edwards and D. G. Lewis

A magnetic investigation of cyanide complexes of nickel(II) in solution. By M. S. Blackie and V. Gold

The stability of the $Ni(CN)_6^{4-}$ ion. By M. S. Blackie and V. Gold

The stability of the $Zn(CN)_4^{2-}$ ion. By M. S. Blackie and V. Gold

Diazonium salt–diazoate equilibria. By R. J. W. Le Fèvre, R. Roper, and I. H. Reece

Metallic complexes of dimethyl-*o*-methylthiophenylarsine. Part III. Complexes of bivalent cobalt. By B. Chiswell and S. E. Livingstone

Chemical constitution and amœbicidal action. Part IV. Synthesis of emetine and stereoisomers of emetine. By M. Barash, J. M. Osbond, and J. C. Wickens

Chemical constitution and amœbicidal action. Part V. Stereochemistry of emetine. By A. Brossi, A. Cohen, J. M. Osbond, P. Plattner, O. Schnider, and J. C. Wickens

Infrared spectra and structure of some simple and bridged nitro-complexes of platinum, palladium, and cobalt. By J. Chatt, L. A. Duncanson, B. M. Gatehouse, J. Lewis, R. S. Nyholm, M. L. Tobe, P. F. Todd, and L. M. Venanzi

Factors influencing the rates of dissociation of metal complexes. Part I. The mechanism of dissociation of mono(ethylenediamine)nickel(II) ion. By A. K. Shamsuddin Ahmed and R. G. Wilkins

Polynucleotides. Part II. Homopolymers of cytidylic and pseudouridylic acid, copolymers with repeating sub-units, and the stepwise synthesis of polyribonucleotides. By A. M. Michelson

Aromatic sulphonation. Part V. Kinetic isotope effects and mechanism. By J. C. D. Brand, A. W. P. Jarvie, and W. C. Horning

Mechanism of the azide–nitrite reaction. Part III. By C. A. Bunton and G. Stedman

Cyclodehydration processes. Part II. Migration of a phenyl group during cyclisation of ω-phenoxyacetophenone. By W. Davies and S. Middleton

Naphthimidazoles. Part II. 5,6,7,8-Tetrahydronaphth[2,3-*d*]imidazole and some of its derivatives. By D. J. Brown and R. J. Harrison

Comparison of some properties of anhydrous sulphuric acid and dideuterosulphuric acid over a range of temperature. By N. N. Greenwood and A. Thompson

The mechanism of electrical conduction in fused phosphoric and trideuterophosphoric acid. By N. N. Greenwood and A. Thompson

Addition compounds of boron trifluoride with orthophosphoric and trideuterophosphoric acid. By N. N. Greenwood and A. Thompson

The reactions of boron halides with anhydrous sulphuric acid: boron tri(hydrogen sulphate) and tetra(hydrogen sulphato)boric acid. By N. N. Greenwood and A. Thompson

β-Aroylpropionic acids. Part XIII. The infrared and ultraviolet spectra of the products of interaction of Grignard reagents with succinic anhydrides, and β-aroylpropionic acids and their esters. By F. G. Baddar and (Mrs.) A. Habashi

Vapour-phase photochemical chlorination and bromination of 2,2,4,4-tetramethylpentane. By J. D. Backhurst

Lactones. Part VI. The preparation of 5,7-dihydroxyphthalide, its 5-methyl ether, and related compounds. By W. R. Allison and G. T. Newbold

Bis-*o*-phenylene pyrophosphite: a new reagent for peptide synthesis. Part II. Some peptide syntheses with the new reagent. By P. C. Crofts, J. H. H. Markes, and H. N. Rydon

Physicochemical studies on starches. Part XVII. The existence of an anomalous amylopectin in starch. By W. Banks and C. T. Greenwood

Some *NN*-di-2-chloroalkyl derivatives of carboxyamides and sulphonamides. By W. C. J. Ross and J. G. Wilson

The dielectric polarisations and apparent dipole moments of alcohols as solutes. By R. J. W. Le Fèvre and A. J. Williams

Dielectric relaxation times for normal alcohols at infinite dilution in carbon tetrachloride or benzene. By R. J. W. Le Fèvre and A. J. Williams

XUM

Molecular polarisability. The photoelectrical measurement of depolarisation factors. The determination of $\infty\delta_2^2$ for six alcohols in carbon tetrachloride. By R. J. W. Le Fèvre and B. Purnachandra Rao.

Molecular polarisability. The anisotropy of the H–O bond in normal alcohols. By C. G. Le Fèvre, R. J. W. Le Fèvre, B. Purnachandra Rao, and A. J. Williams

Molecular polarisability. The molar Kerr constants of seven normal alcohols at infinite dilution in benzene. By R. J. W. Le Fèvre and A. J. Williams

Acid-catalysed rearrangements of alkyl aryl ethers. Part I. Rearrangement of butyl phenyl ethers with aluminium chloride. By M. J. S. Dewar and N. A. Puttnam

Acid-catalysed rearrangements of alkyl aryl ethers. Part II. Rearrangements in the presence of sulphuric–acetic acid mixtures. By M. J. S. Dewar and N. A. Puttnam

Acid-catalysed rearrangements of alkyl aryl ethers. Part III. Rearrangements in the presence of aluminium bromide; the mechanism of such rearrangements. By M. J. S. Dewar and N. A. Puttnam

Phospholipids. Part V. The hydrolysis of the glycerol 1-esters of myoinositol 1- and 2-phosphate. By D. M. Brown, G. E. Hall, and R. Letters

Mechanism and steric course of octahedral aquation. Part I. Aquation of some halogeno- and nitrato-amminebis(ethylenediamine)cobalt(III) ions. By M. L. Tobe

The structure of Floridean starch. Part I. Linkage analysis by partial acid hydrolysis. By S. Peat, J. R. Turvey, and J. M. Evans

The structure of Floridean starch. Part II. Enzymic hydrolysis and other studies. By S. Peat, J. R. Turvey, and J. M. Evans

The barium fluoride–uranium tetrafluoride and strontium fluoride–thorium tetrafluoride systems. By R. W. M. D'Eye and I. F. Ferguson

A molecular-orbital calculation of the ultraviolet absorption spectrum of the quinolizinium cation. By T. E. Peacock

Studies of *Aspergillus niger*. Part XI. Enzymic synthesis of a pseudoaldobiuronic acid. By S. A. Barker, A. Gómez-Sánchez, and M. Stacey

The structure and reactivity of pyridazine quaternary salts. By G. F. Duffin and J. D. Kendall

The Ehrlich–Sachs reaction. Part II. By D. M. W. Anderson and F. Bell

The chemotherapy of schistosomiasis. Part III. *N-p*-Aminophenoxyalkyl-amides, -imides, and -sulphonamides. By J. N. Ashley, R. F. Collins, M. Davis, and N. E. Sirett

Photochemical transformations. Part VI. Photochemical cleavage of cyclohexadienones. By D. H. R. Barton and G. Quinkert

Organosilyloxy-derivatives of metals. Part I. Alkylsilyloxy-derivatives of titanium, zirconium, niobium, and tantalum. By D. C. Bradley and I. M. Thomas

The common-ion effect in the unimolecular solvolysis of t-butyl chloride. By C. A. Bunton and B. Nayak

Structure and reactivity of the oxyanions of transition metals. Part VI. Photolysis of chromate, permanganate, and related compounds in rigid media at low temperatures. By U. Kläning and M. C. R. Symons

The infrared spectra of some compounds containing the trifluoromethylthio-group, $CF_3{\cdot}S{\cdot}$. By S. N. Nabi and N. Sheppard

Nitration of alcohols at oxygen centres. Part I. Criteria for the nitronium-ion mechanism in aqueous solutions of strong acids. By T. G. Bonner and D. E. Frizel

Nitration of alcohols at oxygen centres. Part II. The equilibria established in aqueous sulphuric and perchloric acid and the mechanism of hydrolysis of the nitrate ester. By T. G. Bonner and D. E. Frizel

Nitration of alcohols at oxygen centres. Part III. The reaction of nitric acid and 2,4-dinitrobenzyl alcohol in acetic anhydride–acetic acid. By T. G. Bonner

Steroids. Part XLIII. Comparison of the 16-bromo-17-ketones and 16-bromo-17-hydrins of the 3-unsubstituted and 3β-oxygenated androstane series. By J. Fajkös

Complex halides of the transition metals. Part I. Tetrahedral nickel complexes. By N. S. Gill and R. S. Nyholm

Hydropteridines. Part V. 7,8-Dihydro-6-hydroxypteridine-4-carboxylic acids. By J. Clark and A. J. Layton

Synthesis of dihydronitidine. By K. W. Gopinath, T. R. Govindachari, P. C. Parthasarathy, and N. Viswanathan

The structure and reactivity of triazole quaternary salts. By G. F. Duffin, J. D. Kendall, and H. R. J. Waddington

The anionic polymerisation of vinyl monomers with butyl-lithium. By M. Frankel, A. Ottolenghi, M. Albeck, and A. Zilkha

528. *The Kinetics of the Reaction between Methyl Chloride and Lithium Iodide in Acetone.*

By FARHAT-AZIZ and E. A. MOELWYN-HUGHES.

The rate of chemical reaction between methyl chloride and the iodide ion in acetone has been measured at various temperatures and concentrations in a newly designed reaction vessel which allows the system to be studied in the absence of the vapour. The rate of the reverse reaction is greater than that of the direct reaction by a factor of about 4000, and greater than that found by other workers by a factor of more than 1000.

ACCURATE information has long been available on the kinetics of chemical reactions between polar molecules and ions in solution. New data, of unascertainable accuracy, continue to appear. Many of the reactions studied are of the type $RX + Y^- \longrightarrow RY + X^-$, where R is an alkyl radical, X a halogen atom, and Y^- an anion. They are bimolecular. From the second-order velocity coefficients and the derivatives obtained therefrom, when R is variable while X and Y are constant, several organic theories of chemical " reactivity " have been built. When these reactions take place in water, RX reacts with it, giving an alcohol. When they take place in an alcohol, RX reacts with it to give an ether. Such side reactions with the solvent can be evaded, as Conant and Kirner [1] realised, by using acetone as solvent. If, however, R is any alkyl radical other than methyl, RX in any medium breaks down into HX and an olefin, as Brusoff [2] observed. To avoid both solvolysis and the formation of olefins, one must therefore work with methyl derivatives in a non-hydroxylic medium like acetone.

For these reasons, an attempt was made [3] to study the kinetics of the reaction between methyl bromide and the iodide ion in acetone ($CH_3Br + I^- \longrightarrow CH_3I + Br^-$). Accord- into to current standards, the technique then adopted was crude, but it sufficed to show that the reaction proceeds bimolecularly to an equilibrium at a rate which is about 1000 times faster than in water. The velocity constant decreased as the initial concentration of salt was increased. The gradient of the plot of the logarithm of the velocity constant against ionic strength was shown to be greater than could be accounted for by simple electrostatic theory, and the effect was thought to be due to incomplete ionisation or dissociation of the potassium salts in acetone, but quantitative allowance was not then attempted. The standard kinetic law for opposing second-order reactions was adapted to the case where one of the products was only slightly soluble and its concentration was taken as constant, which cannot be strictly true. In the present extension of this work to the system $CH_3Cl + I^- \rightleftharpoons CH_3I + Cl^-$, heterogeneity has been avoided by the use of lithium instead of potassium salts.

Experimental Materials.—Acetone, of analytical standard, was kept for several days over anhydrous calcium sulphate, and then distilled in an all-glass apparatus with a fractionating column (2·5 cm. diam. × 45 cm. long) filled with glass helices. The b. p. was 56·1°. Values reported by other workers [4] range from 56·1° to 56·3°.

Lithium iodide and chloride were twice crystallised from distilled water and then dried by the technique of Turner and Bissett,[5] which consists of the combined effects of a vacuum, a high temperature and desiccation with phosphoric oxide. Solutions of the salts were made by dissolving them, with agitation, in acetone in conical flasks with male joints fitted with ground glass caps the lower parts of whose joints were greased.

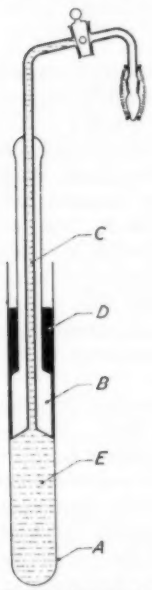
[1] Conant and Kirner, *J. Amer. Chem. Soc.*, 1924, **46**, 232.
[2] Brusoff, *Z. phys. Chem.*, 1900, **34**, 129.
[3] Moelwyn-Hughes, *Trans. Faraday Soc.*, 1949, **45**, 167.
[4] Timmermans, " Physicochemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950.
[5] Turner and Bissett, *Proc. Chem. Soc.*, 1913, **29**, 233.

XUM

The commercial sample of methyl chloride used was pure by spectroscopic and gas-chromatographic standards. A concentrated solution of methyl chloride in acetone was prepared in an absorption pipette and sufficed for the whole investigation.

Commercial methyl iodide was purified by the method of Brown and Acree.[6] The distillate was collected from 42·41° to 42·45°. The boiling points reported by other workers are 42·30—42·36° (Brown and Acree [6]) and 42·50° (Timmermans [4]).

Experimental Method.—A special vessel was designed to permit the reaction to be studied in the absence of the vapour phase and out of contact with mercury (Figure). It consists of a Pyrex glass cylinder (*A*) of 45 mm. bore and 30 cm. length, ground inside, and a ground-glass piston (*B*) with a capillary (2 mm. diam.) outlet (*C*) at the top. Mercury (*D*) poured on the top of the piston acts as a seal, and assists in driving it down. A head of mercury of 7—8 cm. was found suitable.



Vapour-free reaction vessel.

Approximately 300 ml. of lithium iodide solution of known strength were brought up to the working temperature, and then 5 ml. of a strong solution of methyl chloride in acetone were added. The mixture was thoroughly shaken and then poured into the reaction vessel.

The reaction was followed by expressing samples at measured time intervals, chilling them in ice, pipetting 5 ml. into 10 ml. of distilled water and 5 ml. of acetone, adding 5 ml. of 50% sulphuric acid and then titrating the mixture for inorganic iodide against approximately 0·02 molar ceric sulphate solution, ferroin being used as indicator (Lewis [7]).

The initial concentration of lithium iodide was obtained by titration with ceric sulphate at zero time, and (after the removal of organic compounds by evacuation) by titration with silver nitrate with dichlorofluorescein as adsorption indicator at zero time. The latter method is more accurate as it gives the total salt concentration, which is independent of the time of removal of the sample. The initial concentration of inorganic iodide was generally checked twice during the reaction by the silver nitrate method. The latter titrations were performed in the presence of 5 ml. of 2% dextrin solution, as otherwise the end point with a mixture of iodide and chloride is not detectable. Dextrin shifts the end point by a small amount, which can be determined in blank experiments.

The initial concentration of methyl halide was determined by heating known volumes of the reaction mixture with excess of N-sodium hydroxide solution in sealed glass tubes at 100° for 24 hr., and titrating the hydrolysed sample for total halide by the silver nitrate method after neutralising it with acetic acid and boiling it under vacuum, which helps in the detection of the end point.

Kinetic Formulation.—The general evidence on the kinetics of reactions between salts and alkyl halides in hydroxylic media [8] is that the reactions take place entirely between the anions and the organic compounds. The rate of reaction, if there is any, between the undissociated or un-ionised salt and the alkyl halide has been found to be so small as to be insignificant. The same conclusion has later been drawn for these reactions in acetone. Evans and Sugden,[9] for example, find that, though the salt concentration is altered by a factor of 400 in the reaction $n\text{-}C_4H_9Br + LiBr^* \longrightarrow n\text{-}C_4H_9Br^* + LiBr$, the second-order constant for the reaction between the organic compound and the ion does not vary, provided allowance is made for the incomplete dissociation of the salt. For these reasons, and because we have otherwise found it difficult to interpret our results, we have assumed that the reactions taking place are the ionic replacements

$$CH_3Cl + I^- \underset{k_4}{\overset{k_3}{\rightleftharpoons}} CH_3I + Cl^-$$

[6] Brown and Acree, *J. Amer. Chem. Soc.*, 1916, **38**, 2145.
[7] Lewis, *Ind. Eng. Chem. Analyt.*, 1936, **8**, 199.
[8] Moelwyn-Hughes, "The Kinetics of Reactions in Solution," 2nd Edn., Oxford, 1947, pp. 128—130.
[9] Evans and Sugden, *J.*, 1949, 270.

The instantaneous velocity of reaction is consequently

$$-\mathrm{d}[CH_3Cl]_t/\mathrm{d}t = k_2[CH_3Cl]_t[I^-]_t - k_4[CH_3I]_t[Cl^-]_t$$

Denoting by a the initial concentration of methyl chloride, by b the initial concentration of lithium iodide (ionised and un-ionised), by x the concentration of methyl iodide at time t, and by α the degree of ionisation of lithium iodide at time t, we see that

$$[CH_3Cl]_t = a - x$$

$$[I^-]_t = (b - x)\alpha$$

and

$$[CH_3I]_t = x = [LiCl]_t + [Cl^-]_t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The rate law now becomes

$$\mathrm{d}x/\mathrm{d}t = k_2(a - x)(b - x)\alpha - k_4x[Cl^-]_t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Because lithium chloride in acetone is much less ionised than lithium iodide, we can express its ionisation constant as follows:

$$K_1 = [Li^+]_t[Cl^-]_t/[LiCl]_t = [I^-]_t[Cl^-]_t/[LiCl]_t \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

For the same reason, $[LiCl]_t$, according to eqn. (1), is very nearly x. Then $[Cl^-]_t = K_1x(b - x)\alpha$, and eqn. (2) reduces to

$$\frac{\mathrm{d}x}{\mathrm{d}t} = k_2(a - x)(b - x)\alpha - \frac{k_4K_1}{\alpha} \cdot \frac{x^2}{b - x} \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The equilibrium conditions are governed by the equation

$$K = \frac{k_2}{k_4} = \frac{K_1}{\alpha_\infty^2} \frac{x_\infty}{(a - x_\infty)(b - x_\infty)^2} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where x_∞ is the final concentration of methyl iodide. On combining eqns. (4) and (5), we have

$$\frac{\mathrm{d}x}{\mathrm{d}t} = k_2\alpha\left[(a - x)(b - x) - \frac{K_1}{K\alpha^2} \frac{x^2}{(b - x)}\right] \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Because α is a function of the concentration, this equation is not integrable. When α is treated as a constant, there results a highly complicated integrated form, which is not here reproduced. During the course of a run, α varies little from the arithmetic mean of its initial and final values, and the term $K_1/K\alpha^2(b - x)$ has the approximately constant value of $2K_1/K\alpha^2(2b - x_\infty) = W$. These facts allow eqn. (6) to be integrated, giving

$$k_2 = \frac{1}{2\alpha\beta(1 - W)t} \ln\left[\frac{1 - x/(\gamma + \beta)}{1 - x/(\gamma - \beta)}\right] \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where $\gamma = \dfrac{a + b}{2(1 - W)}$ and $\beta = [(a - b)^2 + 4Wab]^{\frac{1}{2}}/2(1 - W)$.

Experimental Results.—In the equilibrium data summarised in Table 1, values marked with an asterisk refer to results obtained from the reverse direction, *e.g.*, the figure 39·41 at 20° stands for the initial concentration of methyl iodide and 43·12 for the total initial concentration of inorganic chloride. The reactions were followed until no further change in the composition of the solution could be detected. About 3 days at 20° and about 1 day at 40° sufficed. Those entries in Table 1 which refer to solutions containing the same initial concentrations of reactants were obtained in purely equilibrium experiments, carried out without studying the kinetics. One and the same solution, kept in the same vessel, was examined for equilibrium concentrations at different temperatures. The ionisation constants are derived from the equation $\ln K_1 = -(31{\cdot}28/\boldsymbol{R}) + (2908/\boldsymbol{RT})$, which was constructured from Serkov's data [10] at 25°, the limiting conductances of Ross Kane,[11] and the temperature coefficients of Blokker.[12] The degrees of

[10] Serkov, *J. Russ. Phys. Chem. Soc.*, 1908, **40**, 413.
[11] Ross Kane, *Ann. Reports*, 1930, **27**, 351.
[12] Blokker, *Rec. Trav. chim.*, 1935, **54**, 975.

XUM

ionisation of lithium iodide have been interpolated or extrapolated from Blokker's figures. The slight increase of K with respect to temperature is adequately summarised by the equation $\ln K = -(11{\cdot}71/\boldsymbol{R}) - (1440/\boldsymbol{RT})$.

TABLE 1. *Equilibrium constants for the reaction* $CH_3Cl + I^- \rightleftharpoons CH_3I + Cl^-$ *in acetone solution*: $K = [CH_3I]_\infty[Cl^-]_\infty/[CH_3Cl]_\infty[I^-]_\infty$.

$t°$(c)	10^5K_1 (moles/l.)	$[CH_3Cl]_0$	$[LiI]_0 + [I^-]_0$ (millimoles/l.)	$[LiI]_\infty + [I^-]_\infty$	α_∞	10^4K
20·00	2·15	44·25	52·26	44·71	0·284	2·08
,,		39·41 *	43·12	34·26	0·305	2·63
,,		16·18	35·39	31·66	0·312	2·47
					Average =	2·37
30·00	1·93	44·25	52·26	43·99	0·280	2·29
,,		39·41 *	43·12	33·62	0·299	2·96
,,		16·67	33·35	29·46	0·309	2·62
,,		44·31	10·64	8·23	0·417	2·16
					Average =	2·47
40·00	1·57	16·43	62·17	55·86	0·255	3·04
,,		44·25	52·26	43·01	0·276	2·72
,,		16·74	30·04	26·04	0·316	2·91
,,		17·75	14·50	12·12	0·381	2·71
,,		44·31	10·64	7·92	0·422	2·50
					Average =	2·76
50·00	1·36	44·25	52·26	42·14	0·273	3·08
,,		17·61	30·96	26·68	0·308	2·76
,,		15·82	31·65	27·57	0·305	2·72
,,		44·31	10·64	7·58	0·408	3·22
					Average =	2·93

TABLE 2. *Bimolecular velocity constants for the reaction* $CH_3Cl + I^- \longrightarrow CH_3I + Cl^-$ *in acetone at* 40·0°; $[CH_3Cl]_0 = 17{\cdot}75$, $[CH_3Cl]_\infty = 15{\cdot}37$ *mmoles/l.*

t (sec.)	$[LiI]_t + [I^-]_t$ (mmoles/l.)	10^3k_2 (l. mole^{-1} sec.$^{-1}$) Completely integrated form of eqn. 6	Eqn. 7	t (sec.)	$[LiI]_t + [I^-]_t$ (mmoles/l.)	10^3k_2 (l. mole^{-1} sec.$^{-1}$) Completely integrated form of eqn. 6	Eqn. 7
0	14·50	—	—	7152	12·43	5·07	4·93
552	14·16	6·58	6·60	1284($t_{\frac{1}{4}}$)	13·91	5·08	5·09
1152	13·95	5·21	5·22	2832($t_{\frac{1}{2}}$)	13·31	5·08	5·09
1752	13·74	4·86	4·87	5136($t_{\frac{3}{4}}$)	12·72	5·07	5·04
2652	13·37	5·08	5·10	∞	12·12	—	—
4152	12·89	5·26	5·26				

Velocity coefficients calculated from the completely integrated form of eqn. 6 are shown in column 3 of Table 2. The calculations are extremely laborious, and, as the figures in column 4 show, lead to values of k_2 which are not significantly different from those obtained by means of the simpler eqn. 7. Both equations have been applied to directly observed points and to values interpolated graphically for times corresponding to 25, 50, and 75% completion.

Velocity coefficients have also been obtained by using eqn. 6 in the incremental form. This method, though mathematically not so exact, is physically superior, because no assumption is necessary concerning α, and its exact value can be used for each composition. Values of k_2 obtained in this way are approximately 10% higher than those obtained by the other two methods, and are accepted as being the most reliable.

Runs have been repeated with various initial concentrations of methyl and lithium halides and, although they give slightly different values, there is no discernible trend. Within the limit of accuracy attained, there is no evidence that k_2 or k_4 is affected by initial concentration of electrolyte or of methyl halide (see Table 3). No general answer can be given to the question of whether un-ionised molecules of the alkali halides react with methyl halides in acetone solution. In the present system, however, such a supposition is not necessary, although it cannot, without further study, be ruled out.

A summary of the mean values of k_2 obtained from all the runs is given in Table 4. The k_4 values were derived from them by means of eqn. (5), and are to some extent dependent on the adopted values of K_1. Had we accepted the K_1 values of Blokker [12] rather than those of Serkov,[10] the absolute values of k_4 would be lower by a factor of about 2.

TABLE 3. *The influence of initial concentrations (in mmoles/l.) on the bimolecular velocity constant (k_2 in l. mole^{-1} sec.$^{-1}$) at 40·0°.*

$a = [CH_3Cl]_0$	$b = [LiI]_0 + [I^-]_0$	10^3k_2	$a = [CH_3Cl]_0$	$b = [LiI]_0 + [I^-]_0$	10^3k_2
17·8	14·5	6·25	30·4	31·0	6·80
16·7	30·1	6·11	16·4	62·2	6·74

TABLE 4. *Bimolecular velocity constants (in l. mole^{-1} sec.$^{-1}$) for the reactions* $CH_3Cl + I^- \longrightarrow CH_3I + Cl^-$ *(k_2) and* $CH_3I + Cl^- \longrightarrow CH_3Cl + I^-$ *(k_4) in acetone solution.*

	10^4k_2				10^4k_2		
t°	obs.	calc.	k_4	t°	obs.	calc.	k_4
20·0	8·08	8·96	3·85	40·0	65·2	63·7	23·3
30·0	24·8	24·8	9·82	50·0	157	157	53·5

Temperatures were maintained constant to with ±0·03°. The Arrhenius equations are

$$k_2 = 2{\cdot}14 \times 10^{10} \exp(-17{,}950/\boldsymbol{R}T) \text{ and } k_4 = 7{\cdot}78 \times 10^{12} \exp(-16{,}510/\boldsymbol{R}T)$$

It will be observed that k_4 is about 4000 as great as k_2, and that the difference in rates is reflected chiefly in the pre-exponential constants.

Comparison with Other Work.—The kinetic results of Hughes, Ingold, and Mackie [13] on the reaction $CH_3I + Cl^- \longrightarrow CH_3Cl + I^-$ in acetone are not directly comparable with ours. They used sealed ampoules with an unspecified volume of vapour; our system was studied in the absence of the vapour phase. This difference in technique, however, is not comparable with the difference in interpretations or capable of explaining the difference in the quantitative conclusions. (1) They make no allowance for the reverse reaction, and state that a decrease observed by them in their bimolecular constant as the reaction proceeds is " of the wrong form to be ascribed to reversibility." The reverse reaction is therefore dismissed. We, on the other hand, not only find that the facts are readily explained in terms of the standard kinetic treatment of opposing bimolecular reactions but have shown, by adding lithium iodide to methyl chloride, that the reverse reaction does, in fact, take place. The treatment for opposing bimolecular reactions satisfactorily fits the facts, and no drift can be detected in either velocity coefficient. (2) They claim that the reaction is subject to a salt effect, which is said to be generic to Finkelstein substitutions, negative in sign, and specific with respect to the cation. We, on the other hand, find that the bimolecular constant, computed with allowance for the reverse reaction, is unaffected, within the regions examined, by the concentration of electrolyte or methyl halide. (3) They treat lithium chloride in acetone solution as completely ionised (or dissociated) whereas, in the instance cited by them, 98% of the salt is un-ionised (or undissociated). (4) Their runs, with one exception, have been carried out in the presence of approximately 0·1N-lithium perchlorate. That the presence of this salt should decrease the apparent second-order constants can be explained in terms of its suppression of the ionisation of lithium chloride; that it should cause the drift in their constant to disappear is a result which is difficult to interpret.

Owing to their permitting the escape of the vapours of methyl iodide and methyl chloride into the free gas space in contact with their solutions, not allowing for the kinetic consequences of the reverse reaction, and neglecting the association of lithium and chloride ions, the bimolecular constants given by Ingold, Hughes, and Mackie for the reaction $CH_3I + Cl^- \longrightarrow CH_3Cl + I^-$ are more than 1000 times smaller than ours.

We are indebted to the Royal Commission for the Exhibition of 1851 for the award of an Overseas Scholarship, to Mr. Riaz-ud-Din for the complete integration of eqn. 6, and to Mr. F. Webber for making the new reaction vessel.

DEPARTMENT OF PHYSICAL CHEMISTRY, CAMBRIDGE. [*Received, October 30th*, 1958.]

[13] Hughes, Ingold, and Mackie, *J.*, 1955, 3177.

XUM

529. *The Kinetics of the Reaction between Methyl Iodide and Potassium Cyanide in Aqueous Solution.*

By B. W. Marshall and E. A. Moelwyn-Hughes.

The reaction between methyl iodide and potassium cyanide in aqueous solution is shown to be irreversible, bimolecular, and free from complications. The Arrhenius equation is $\ln k_2$ (l. mole^{-1} sec.$^{-1}$) $= 26{\cdot}284 - 19{,}990/RT$.

Experimental.—The kinetics of formation of nitriles from alkyl halides and potassium cyanide in aqueous solution have not hitherto been studied. The reaction $CH_3I + CN^- \longrightarrow CH_3CN + I^-$ has now been studied in aqueous solution in the absence of the vapour in the new reaction vessel.[1] Solutions of methyl iodide were made up in conductivity water that had been freed from dissolved gases; known volumes of the solution, about 475 ml., were then kept in the thermostat, and about 25 ml. of a standard solution of potassium cyanide were added from a burette to make the total volume of solution exactly 500 ml. The solutions were thoroughly mixed and immediately transferred to the reaction vessel. Samples were removed at regular intervals and immediately analysed for cyanide or iodide ion. The temperature of the system remained constant to within 0·01° c in individual runs, and to within 0·03° c in different runs.

Methyl iodide was purified by the same method and to the same standard as that used by earlier workers in this Department. Distilled water which had been passed through Amberlite ion-exchange and thoroughly out-gassed by vigorous boiling under reduced pressure was used in making up the solutions required for the kinetic studies. "AnalaR" (B.D.H) potassium cyanide was shaken with ethyl alcohol, washed with ether, and dried in a vacuum desiccator during the initial work, until it was confirmed that the use of the same material without further purification had no effect on the rate constant.

Analytical Methods.—Samples of the solution were analysed for both cyanide and iodide ions by standard argentometric methods. The former was measured by Liebig and Denigés's method under the conditions recommended by Kolthoff,[2] the titration being sensitive to within 0·05 ml. of 0·01N-silver nitrate. Iodide ion was estimated after removing free cyanide as a soluble cyanohydrin with formalin, as described by Kolthoff and Stenger.[4]

The initial concentration of methyl iodide was measured by determining the iodide ion liberated when samples of the reaction mixture were allowed to react to completion in Pyrex ampoules in an oven at 100°. It was also necessary to estimate the concentration of acetonitrile at the end of a run to discover how much methyl isocyanide, if any, had been formed. This was quite easily done, since it is stable to alkali, while acetonitrile is readily hydrolysed, giving ammonia as the only volatile product.

Cyanide ion, which also gives ammonia on hydrolysis, was removed from the samples, which had been allowed to react to completion in the thermostat, by titration with silver nitrate to a clear point. After thorough washing of the precipitate, the filtrate and washings were gently refluxed with 5N-sodium hydroxide for 2 hr., and then vigorously boiled for 30 min. to transfer all the liberated ammonia into the absorption solution of 4% boric acid. The absorbed ammonia was then titrated against standard hydrochloric acid, methyl red being used as indicator. The

Table 1. *Estimated amounts of acetonitrile formed.*

By ammonia liberated in hydrolysis (mmoles/l.)	35·50	35·55
By iodide ion liberated in the reaction (mmoles/l.)	34·95	35·05
Blank (mmole/l.)	0·75	0·60

difference between the amount of acetonitrile formed and the amount of methyl iodide consumed was negligible, *i.e.*, comparable in magnitude with the results of blank experiments carried out on solutions containing cyanide ion but no acetonitrile; hence no isocyanide is formed under these conditions (see Table 1).

[1] Farhat-Aziz and Moelwyn-Hughes, preceding paper.
[2] Fahim and Moelwyn-Hughes, *J.*, 1956, **214**, 1034.
[3] Kolthoff and Stenger, "Volumetric Analysis," Interscience, New York, 2nd Edn., 1947, Vol. 2, pp. 282—283.
[4] *Op. cit.*, pp. 266—267.

XUM

Kinetic Scheme.—In principle, at least six reactions can take place:

$$CH_3I + CN^- \longrightarrow CH_3{\cdot}CN + I^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$
$$CH_3I + CN^- \longrightarrow CH_3{\cdot}NC + I^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$
$$CH_3I + H_2O \longrightarrow CH_3{\cdot}OH + H^+ + I^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$
$$CH_3I + OH^- \longrightarrow CH_3{\cdot}OH + I^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$
$$CH_3{\cdot}CN + 2H_2O \longrightarrow CH_3{\cdot}CO_2NH_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$
$$CN^- + H_2O \longrightarrow HCN + OH^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Reaction (1) goes to completion, and reaction (2) does not occur under the conditions employed. The known rates of reactions (3) and (4) as measured by Moelwyn-Hughes [5] are so much less than the rate of reaction (1) as to be negligible in this study; this fact is consistent with the impossibility of differentiating between the constants calculated from the rate of liberation of iodide ion and those calculated from the rate of consumption of cyanide ion (see Table 2).

The hydrolysis of acetonitrile, reaction (5), would not affect the kinetic analysis, but might have affected the static analysis of the product. Separate experiments with aqueous solutions of acetonitrile alone, however, showed that the rate of hydrolysis was extremely slow, even at 85°, and of no significance in the temperature range employed. The hydrolysis of the cyanide ion, reaction (6), may well be so rapid as to establish equilibrium throughout. Whether this is true or not, a solution containing 150 mmoles/l. of potassium cyanide showed that the extent of hydrolysis was less than 1%. For this reason a correction was not applied for the difference between the concentrations of total cyanide and of cyanide ion.

Results.—In runs followed up to 90% completion the rate constants, as calculated from the ordinary equation for an irreversible second-order reaction, showed no tendency to drift. No variation of rate constant with initial concentration of potassium cyanide was found when this

TABLE 2.

Run at 41·24° C = 314·40° K; $a = [CH_3I]_0 = 25{\cdot}77$ mmoles/l.; $b = [CN^-]_0 = 39{\cdot}10$ mmoles/l.; $k_2 = 3{\cdot}37 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$. Unit of concentration = mmole/l.

t (min.)	$[CN^-]$ obs.	$[I^-]$ obs.	$[CN^-]$ calc.	$[I^-]$ calc.	t (min.)	$[CN^-]$ obs.	$[I^-]$ obs.	$[CN^-]$ calc.	$[I^-]$ calc.
0·0	39·10	—	39·10	0·0	210·0	21·55	—	21·32	17·78
15·5	—	2·65	36·45	2·89	240·0	—	18·74	20·38	18·72
36·0	33·05	—	33·16	5·94	270·0	19·65	—	19·58	19·52
55·0	—	8·08	30·87	8·23	300·0	—	20·30	18·82	20·28
75·0	28·90	—	28·88	10·22	325·0	18·45	—	18·39	20·65
95·0	—	11·83	27·25	11·87	350·0	—	21·15	17·94	21·16
116·0	25·60	—	25·74	13·36	386·0	17·60	—	17·39	21·71
135·0	—	14·47	24·62	14·48	421·0	—	22·20	16·93	22·17
155·0	23·70	—	23·57	15·53	450·0	16·60	—	16·59	22·51
180·0	—	16·63	22·46	16·64	∞	—	25·77	13·33	25·77

TABLE 3. *The effect on the rate constant at* 318·46° K *of varying the potassium cyanide concentration and of adding potassium nitrate.*

[KCN] (mmoles/l.)	30·22	49·92	50·0	50·0	99·54	50·0
[KNO_3] (mmoles/l.)	0	0	0	10	0	100
10^3k_2 (l. mole^{-1} sec.$^{-1}$)	5·02	5·07	4·92	5·15	4·94	5·09

TABLE 4.

T (°K)	293·26	300·05	305·32	309·87	314·40	318·46	323·00	327·43
10^4k_2 (l. mole^{-1} sec.$^{-1}$), obs.	3·27	7·21	13·3	21·7	33·8	50·3	82·2	127·0
,, ,, calc.	3·36	7·44	13·1	21·6	33·9	51·2	79·7	122·0

concentration was varied from 30 to 150 mmoles/l., nor did the addition of up to 100 mmoles/l. of potassium nitrate produce any systematic change in the rate of reaction. A specimen set of data for one run, analysed for iodide and cyanide ions alternately, is shown in Table 2, together

[5] *Proc. Roy. Soc.*, 1953, *A*, **220**, 286—296; 1949, *A*, **196**, 540.

XUM

with the calculated values of the two ionic concentrations at each point. The influence of the initial concentrations is shown in Table 3. The velocity coefficients remained constant to within 2% from run to run. Values of the rate constant, k_2, at different temperatures have been fitted by the method of least squares to a straight-line plot of $\log_{10}k_2$ against $1/T$. Table 4 gives a comparison of the mean measured values of k_2 with those calculated from the Arrhenius equation. Observed and calculated values agree to within $\pm 4\%$. The probable error in the apparent energy of activation is ± 70 cal./mole.

We are indebted to British Celanese Ltd. for the award of a research studentship.

DEPT. OF PHYSICAL CHEMISTRY, CAMBRIDGE. [*Received, October 30th*, 1958.]

---

530. *The Kinetics of Certain Ionic Exchange Reactions of the Four Methyl Halides in Aqueous Solution.*

By R. H. BATHGATE and E. A. MOELWYN-HUGHES.

The kinetics of six reactions of the type $CH_3X + Y^- \longrightarrow CH_3Y + X^-$, mostly involving fluorine, have been studied in aqueous solution. The apparent energies of activation have been compared with the energies estimated for partial de-solvation of the ion and the polar molecule. Many more data than we now possess are needed before a satisfactory theory of the kinetics of simple substitutions at the saturated carbon atom can be developed. This paper provides some new material, chiefly on the rates at which the fluoride ion attacks the other methyl halides in aqueous solution under vapour-free conditions.

Preparation and Purity of Reactants.—The commercial sample of methyl chloride used was found on analysis to be 99·8% pure. No impurities could be detected by infrared absorption spectroscopy. Methyl bromide was purified as described by Egan and Kemp.[1] Its vapour pressure at 0° was 664·55 mm. (cf. 660·4 mm. found by them). Methyl iodide was purified by Brown and Acree's method.[2] Its boiling point was 42·42° (cf. 42·36° recorded by Timmermans [3]). Methyl fluoride was prepared and purified as described by Glew and Moelwyn-Hughes.[4] Its vapour pressure was 754 mm. at the sublimation point of carbon dioxide (cf. the value of 756 mm. given by them). Water was purified by distillation and by passage through Amberlite ion-exchange resin No. MB3.

Methods of Analysis.—Hydrogen ion was determined by titration with standard potassium hydroxide solution, with nitrogen bubbling through to remove dissolved carbon dioxide. The end-point was determined either by using bromothymol blue as indicator, or by following the pH electrometrically. Iodide ion was determined by titration with standard potassium iodate, as described by Moelwyn-Hughes.[5] Fluoride ion was determined by Grant and Haendler's method [6] of titration with thorium nitrate and determining the position of the end-point by use of a high-frequency titrimeter.[7,8] The total concentration of ionic halide, excluding fluoride, was found by titration with standard silver nitrate, dichlorofluorescein being used as indicator. 5 ml. of a 2% solution of dextrin were added to the titration solution to prevent premature precipitation of the silver halide. It was found that this displaced the end-point slightly, by an amount for which quantitative correction was made. The correction is greater in the presence of fluoride ion.

Kinetic Procedure.—About 400 ml. of the solution of the potassium halide were sucked into a gas pipette and degassed by boiling at room temperature for a few minutes. An appropriate

[1] Egan and Kemp, *J. Amer. Chem. Soc.*, 1938, **60**, 2097.
[2] Brown and Acree, *ibid.*, 1916, **35**, 2145.
[3] Timmermans, " Physico-chemical Constants of Pure Organic Compounds," Elsevier, New York, 1950.
[4] Glew and Moelwyn-Hughes, *Proc. Roy. Soc.*, 1952, *A*, **211**, 254.
[5] Moelwyn-Hughes, *ibid.*, 1953, *A*, **220**, 386.
[6] Grant and Haendler, *Ind. Eng. Chem. Anal.*, 1956, **28**, 415.
[7] Blaedel, Malmstadt, Petitjean, and Anderson, *ibid.*, 1952, **24**, 1240.
[8] Hall, *ibid.*, p. 1236.

amount of methyl halide was introduced either from a gas burette or from a graduated pipette and mixed by shaking. The mixture was then quickly sucked into a vapour-free reaction vessel of the type described by Fahim and Moelwyn-Hughes.[9] The time of starting the reaction was taken as the time when one half of the reaction mixture had entered the vessel. The vessel was kept in a water thermostat, maintained constant to within 0·03° by a mercury–toluene thermoregulator with a Sunvic relay. Temperatures were measured by a mercury-in-glass thermometer graduated in tenths of a degree and compared with a thermometer calibrated by the National Physical Laboratory. The absolute zero of temperature was taken as −273·16° c.

Samples were removed from the vessel at measured intervals of time, chilled in ice-water, and analysed for inorganic halides. When the reaction was relatively fast, infinity values were found by following it until no further change took place. When this was not practicable, measured samples were sealed in glass ampoules with an equal volume of N-sodium hydroxide when the reaction was about three-quarters complete, and digested at 100° until the methyl halide was completely hydrolysed; the contents of the ampoule were then analysed for the appropriate halide ion. This method could not be used to determine the concentration of methyl fluoride, as the high concentration of hydroxide interferes with the estimation of fluoride ion. Therefore with reactions involving methyl fluoride, samples were sealed in glass ampoules without sodium hydroxide, and digested at 100° for long enough to ensure the complete hydrolysis of the methyl fluoride.

Kinetic Formulation.—The general scheme for the system of reactions here studied can be described as follows:

$$\begin{array}{ccc} CH_3X + Y^- & \underset{k_4}{\overset{k_3}{\rightleftharpoons}} & CH_3Y + X^- \\ \downarrow k_1 & & \downarrow k_2 \\ CH_3{\cdot}OH + H^+ + X^- & & CH_3{\cdot}OH + H^+ + Y^-, \end{array}$$

where X and Y represent halogen atoms.

There are three special cases to be considered.

(1) When both hydrolyses can be ignored, we have *

$$k_2 = \frac{1}{2(1-K)\beta t} \ln\left[\frac{1 - x/(\alpha+\beta)}{1 - x/(\alpha-\beta)}\right] \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $K = k_4/k_2$, $\alpha = (a+b)/2(1-K)$, and $\beta = [(a-b)^2 + 4Kab]^{\frac{1}{2}}/2(1-K)$.

Here a and b are the initial concentrations of CH_3X and Y^-, respectively. This equation has been found applicable at temperatures below 350° K when X = Cl and Y = I.

(2) When $d[Y^-]/dt$ is zero, $d[X^-]/dt = d[H^+]/dt$, and $[CH_3Y] = k_2[CH_3X][Y^-]/(k_3 + k_4[X^-])$.

The rate equation then becomes

$$\frac{dx}{dt} = k_1(a-x) + \frac{k_2(a-x)(b-x)}{1 + (k_4/k_3)x}$$

and the observed first-order constant is consequently

$$k = k_1 + \frac{k_2(b-x)}{1 + (k_4/k_3)x} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

These simple conditions correspond very nearly to those found when X = F and Y = I.

(3) When the reverse reaction can be ignored, terms involving k_4 can be omitted, and the differential form of the rate equation is

$$dx/dt = k_1(a-x) + k_2(a-x)(b-x)$$

---

* This equation is identical with eqn. 7 (p. 2644) except that, at the suggestion of a referee, we have used γ for α in the earlier equation.

[9] Fahim and Moelwyn-Hughes, *J.*, 1956, 1034.

XUM

which can be readily integrated. It has been shown that the first-order constant is

$$k = k_1 + k_2(b - x),$$

or, if $b \gg a$,

$$k = k_1 + k_2 b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

These conditions tally with those found when X is Cl, Br, or I, and Y = F.

The Reactions between Methyl Chloride and Potassium Iodide and between Methyl Iodide and Potassium Chloride in Aqueous Solution.—The ratio $k_4/k_2 = K$ was first determined for this system by ascertaining the position of the minimum concentration of the halide ion originally present, for two runs started in opposite directions at the same temperature, as described by Moelwyn-Hughes.[10] Values of K thus found were constant to within $\pm 10\%$ while a/b was changed fourfold. The observed values of K at different temperatures in the region where

TABLE 1.

T (°K)	323·11	333·04	343·70
K (obs.)	0·210	0·211	0·250
K (calc.)	0·205	0·224	0·245

this treatment is applicable are shown in Table 1, where they are compared with values calculated from the equation

$$K = 3{\cdot}89 \exp(-1900/\boldsymbol{RT}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The calculated values of K were used in determining k_2 and k_4 by means of eqn. (1), which yielded reliable results for reactions starting with methyl chloride and potassium iodide. In reactions started with methyl iodide and potassium chloride, hydrolysis is appreciable even in

TABLE 2.

$a = [CH_3Cl]_0 = 40{\cdot}47$ mmoles/l., $b = [KI]_0 = 80{\cdot}85$ mmoles/l., $T = 333{\cdot}04°$ K, $k_2 = 7{\cdot}55 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$, $k_4 = 1{\cdot}69 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$.

t (min.)	0	40	80	150·5	220	310	∞
x (obs.)	0	4·23	8·47	14·86	19·72	24·12	40·47
x (calc.)	0	4·58	8·90	14·47	19·48	29·40	40·47

the early stages of the reaction. A typical run is shown in Table 2, the entries in the last column of which were calculated from the equation

$$x = ab/(1 - K)\{\alpha + \beta \coth[(k_2 - k_4)\beta t]\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

k_2 and k_4 were found to vary by $\pm 3\%$ at a given temperature while a/b was varied by a factor of 4. Values at different temperatures are shown in Table 3, together with those calculated from the equations

$$k_2 = 9{\cdot}55 \times 10^9 \exp(-20{,}020/\boldsymbol{RT}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$k_4 = 4{\cdot}17 \times 10^{10} \exp(-21{,}970/\boldsymbol{RT}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

The standard deviation of the apparent activation energies is ± 300 kcal./mole.

TABLE 3.

T (°K)	323·11	333·04	343·70	353·60	366·02
$10^4 k_2$ (l. mole^{-1} sec.$^{-1}$), obs.	2·79	7·51	18·8	37·7	111
,, ,, calc.	2·75	6·92	17·8	40·7	107
$10^4 k_4$ (l. mole^{-1} sec.$^{-1}$), obs.	0·57	1·68	4·60	9·97	31·9
,, ,, calc.	0·59	1·62	4·57	11·2	31·6

The Reaction of Methyl Fluoride with Potassium Iodide, and the Reactions of Potassium Fluoride with Methyl Chloride, Methyl Bromide, and Methyl Iodide in Aqueous Solution.—The reactions

$$CH_3F + I^- \longrightarrow CH_3I + F^-;\ CH_3Cl + F^- \longrightarrow CH_3F + Cl^-;$$

$$CH_3Br + F^- \longrightarrow CH_3F + Br^-;\ \text{and}\ CH_3I + F^- \longrightarrow CH_3F + I^-$$

were found to be of pseudo-first order. This is so for the first-mentioned reaction because the methyl iodide produced is hydrolysed rapidly enough to keep the concentration of the iodide ion

[10] Moelwyn-Hughes, *J.*, 1938, 779.

effectively constant. In the other three reactions it is necessary to use fluoride ion at a concentration about fifty times that of the methyl halide in order that the ionic exchange should not be masked by hydrolysis. Under these conditions, it is the concentration of fluoride ion which remains appreciably constant. The reaction $CH_3F + I^- \longrightarrow CH_3I + F^-$ was followed by estimation of the acid produced by hydrolysis, which, as is shown below, is approximately equal to the concentration of fluoride ion under the experimental conditions. This reaction showed the greatest deviation of the four from pseudo-first-order kinetics, and, in agreement with eqn. (2), the apparent first-order constant was found to decrease as the reaction proceeded. The results of a typical run for each of the four reactions are shown in Tables 4—7 in which k is the apparent first-order constant governing the production of halide or hydrogen ion.

TABLE 4.

$[CH_3F]_0 = 19{\cdot}2$ mmoles/l., $[KI]_0 = 80{\cdot}04$ mmoles/l., $T = 343{\cdot}54°$ K, $k = 5{\cdot}78 \times 10^{-7}$ sec.$^{-1}$

t (min.)	1,196	5,725	13,078	28,955	69,160
x (obs.)	0·60	3·73	6·79	12·17	15·56
x (calc.)	0·93	3·53	7·03	12·31	17·46

TABLE 5.

$[CH_3Cl]_0 = 16{\cdot}83$ mmoles/l., $[KF]_0 = 971$ mmoles/l., $T = 343{\cdot}74°$ K, $k = 1{\cdot}488 \times 10^{-5}$ sec.$^{-1}$

t (min.)	110	212	310	537	1,265	1,530	1,742
x (obs.)	1·28	2·56	3·72	6·20	11·17	12·46	13·19
x (calc.)	1·22	2·53	3·77	6·16	11·27	12·15	13·19

TABLE 6.

$[CH_3Br]_0 = 29{\cdot}16$ mmoles/l., $[KF]_0 = 971$ mmoles/l., $T = 313{\cdot}28°$ K, $k = 5{\cdot}67 \times 10^{-6}$ sec.$^{-1}$

t (min.)	122	406	1,150	1,380	1,545
x (obs.)	0·74	3·43	9·11	10·66	11·64
x (calc.)	0·76	3·38	9·12	10·64	11·64

TABLE 7.

$[CH_3I]_0 = 19{\cdot}12$ mmoles/l., $[KF]_0 = 942$ mmoles/l., $T = 363{\cdot}86°$K, $k = 4{\cdot}33 \times 10^{-4}$ sec.$^{-1}$

t (min.)	10	20	30	40	50	60	80	215
x (obs.)	2·30	6·50	8·96	11·52	13·02	14·60	16·34	18·86
x (calc.)	2·33	6·17	9·15	11·41	13·19	14·54	16·40	18·90

Values of k, k_1, $[X^-]$, and k_2 for various temperatures are given in Tables 8—11. Values of k_1 in Table 8 were taken from Glew and Moelwyn-Hughes,[4] and in Tables 9—11 from Moelwyn-Hughes.[5] The Arrhenius equations for the variation of k_2 with respect to temperature, and the

TABLE 8. $CH_3F + I^- \longrightarrow CH_3I + F^-$.

T (°K)	10^7k (sec.$^{-1}$)	10^7k_1 (sec.$^{-1}$)	$[I^-]$ (moles/l.)	10^6k_2 (l. mole^{-1} sec.$^{-1}$) obs.	calc.
333·3	13·2	1·24	1·025	1·16	1·25
343·5	5·78	2·59	0·080	4·0	3·52
353·8	99	7·04	1·002	9·2	9·33
363·7	38	18·8	0·080	24	22·8
363·8	228	18·8	1·008	21	23·1

$k_2 = 1{\cdot}65 \times 10^9 \exp(-23{,}060/RT)$

TABLE 9. $CH_3Cl + F^- \longrightarrow CH_3F + Cl^-$.

T (°K)	10^6k (sec.$^{-1}$)	10^6k_1 (sec.$^{-1}$)	$[F^-]$ (moles/l.)	10^6k_2 (l. mole^{-1} sec.$^{-1}$) obs.	calc.
323·32	13·43	8·60	0·981	4·92	5·25
343·74	148·8	80·6	0·971	70·2	67·6
366·25	1472	765	1·001	707	776

$k_2 = 7{\cdot}36 \times 10^{11} \exp(-26{,}900/RT)$

TABLE 10. $CH_3Br + F^- \longrightarrow CH_3F + Br^-$.

T (°K)	10^7k (sec.$^{-1}$)	10^7k_1 (sec.$^{-1}$)	$[F^-]$ (moles/l.)	10^7k_2 (l. mole^{-1} sec.$^{-1}$) obs.	calc.
313·28	5·67	3·43	0·971	2·31	2·69
333·14	62·7	35·2	0·915	30·1	27·5
353·53	480	271	0·910	229	263
366·18	1755	903	0·994	857	851

$k_2 = 9{\cdot}12 \times 10^{11} \exp(-25{,}200/RT)$

XUM

values of k_2 at the experimental temperatures calculated therefrom, are also given in Tables 8—11.

TABLE 11. $CH_3I + F^- \longrightarrow CH_3F + I^-$.

T (°K)	10^6k (sec.$^{-1}$)	10^6k_1	[F$^-$] (moles/l.)	10^5k_2 (l. mole^{-1} sec.$^{-1}$) obs.	calc.
323·74	4·81	2·92	0·863	2·04	2·19
343·74	43·6	27·3	0·842	20·9	19·5
363·86	433	279	0·942	162	163

$k_2 = 2{\cdot}09 \times 10^{11} \exp(-25{,}200/RT)$

TABLE 12. *Constants of the Arrhenius equation* $\log_{10}k_2$ (*l. mole*$^{-1}$ *sec.*$^{-1}$) $= \log_{10}A - E_A/2{\cdot}303RT$ *for substitutions of the methyl halides in water, and calculated values of the energies of activation.*

Reactants	$\log_{10}A$	E_A	E	Reactants	$\log_{10}A$	E_A	E
$CH_3Cl + F^-$	11·9	26·9	25·9	$CH_3F + I^-$	9·1	22·9	17·70
$CH_3Br + F^-$	12·0	25·2	25·8	$CH_3Cl + I^-$	9·9	20·0	17·8
$CH_3I + F^-$	11·3	25·2	25·6	$CH_3Br + I^-$	10·2	18·3 [10]	17·7
				$CH_3I + I^-$	9·5	17·7 [13]	17·5
$CH_3F + Cl^-$	7·7	22·2 [11]	23·7				
$CH_3Br + Cl^-$	12·8	24·7 [12]	23·7	$CH_3F + OH^-$	9·6	21·6 [4]	22·5
$CH_3I + Cl^-$.....	10·6	22·0	23·5	$CH_3Cl + OH^-$	12·6	24·3 [14]	22·6
				$CH_3Br + OH^-$	13·0	23·0 [14]	22·6
$CH_3Cl + Br^-$	14·1	27·8 [13]	21·2	$CH_3I + OH^-$	12·1	22·2 [14]	22·3
$CH_3I + Br^-$	9·8	19·3 [10]	20·9				

Discussion.—Reference can be made here to but a few theories. Ogg and Polanyi,[15] in adapting to reactions between ions and polar molecules in solution the theory of Heitler and London [16] for reactions between atoms and non-polar molecules in gases, naturally allowed for the work required to de-solvate the ion, and estimated the energy of activation by finding the point of intersection of the potential energy curves of the systems $CH_3X + Y^-$ and $CH_3Y + X^-$. Their conclusion, which numerically has been confirmed,[17] is that the energy of activation is expended in increasing the bond length of the molecule and in overcoming its intrinsic repulsion to the ion. The idea that activation in these reactions corresponds roughly with the critical interaction energy of an ion-dipole pair has since been more directly expressed,[14] and statistical allowance has been made for the effect of the axially symmetrical field of the dipole on approach of the ion.[18] Despite simplification and improvement, however, and the ease with which steric hindrance effects can be ascribed to additional repulsions, Ogg and Polanyi's theory leads to energies of activations which are far too large, and reflect a dependence on bond energies which is not supported by experiment.

Hurst and Moelwyn-Hughes [19] base their treatment of the gaseous reaction $CH_3X + Y^- \longrightarrow CH_3Y + X^-$ on Born and Heisenberg's theory of polar diatomic molecules.[20] The reacting molecule and ion are regarded as a tripole $[X{\cdot}CH_3{\cdot}Y]^-$, and the reaction as the gradual transference of the electronic charge from X to Y. As in the theories of Heitler and London and of Ogg and Polanyi, only linear combinations are considered. Repulsions are ascribed in part to Coulombic forces, but mainly to intrinsic interactions of closed shells of electrons. Attractions are attributed to Coulombic and polarisation

[11] Fahim, *Dissertation*, Cambridge, 1955.
[12] Holland, *Dissertation*, Cambridge, 1954.
[13] Swart and LeRoux, *J.*, 1956, 2110.
[14] Moelwyn-Hughes, *Proc. Roy. Soc.*, 1949, *A*, **196**, 540.
[15] Ogg and Polanyi, *Trans. Faraday Soc.*, 1935, **31**, 604.
[16] Heitler and London, *Z. Physik*, 1927, **44**, 457.
[17] Moelwyn-Hughes, *Acta Physicochim. U.S.S.R.*, 1936, **4**, 173.
[18] Kacser, *J. Phys. Chem.*, 1952, **56**, 1101.
[19] 2° *Corso di Chimica, Varenna, Ed. Accademia dei Lincei*, 1957; Hurst, Dissertation, Cambridge, 1948.
[20] Born and Heisenberg, *Ann. Physik*, 1916, **49**, 229.

forces. Numerical constants governing the repulsions and attractions exerted between the three ionic pairs are derived from the polarisabilities and the energies of ionisation of the ions and the dipole moments of the molecules. According to this treatment, no energy of activation is necessary, in the gas, for symmetrical reactions of the type $CH_3X + X^- \longrightarrow CH_3X + X^-$, because the intermediate complex $[X{\cdot}CH_3{\cdot}X]^-$ has less energy, and is therefore more stable, than the isolated pair $X{\cdot}CH_3$ and X^-. If the theory is sound and the numerical constants reliable, it follows, for example, that the replacement $CH_3F + F^- \longrightarrow CH_3F + F^-$ in the gas should take place at every collision, since the critical intermediate $[F{\cdot}CH_3{\cdot}F]^-$ is stable (cf. the stability of the ion $[F{\cdot}H{\cdot}F]^-$). Only highly endothermic substitutions would require an energy of activation. How is it, then, that these reactions in solution are, on the basis of one chemical change for one collision, so slow? It would appear that the rôle of the solvent in reactions between ions and polar molecules is to impede the reaction, and to render measurable in solution a rate which would be immeasurably fast in the gas. This conclusion concerning reactions between ions and polar molecules is sharply contrasted with that reached by Hinshelwood [21] and Moelwyn-Hughes [22] in the many bimolecular reactions which they investigated between electrically uncharged molecules in the gaseous phase and in non-polar solvents.

The theory can be applied without much conjecture or computation.

Each ion in solution, as in crystalline hydrates, is surrounded by solvent molecules, of number c, to which it adheres with a known tenacity. If the chemical reaction of such a solvated ion with a molecule in solution necessitates its partial exposure, it must rid itself of at least one of the solvent molecules forming its sheath, and present itself to the molecule it seeks to attack with only $c - 1$ solvent molecules around it. The ratio of the concentration, n^*, of such partly de-solvated ions to the concentration, n, of completely solvated ions is proportional to the Boltzmann factor $\exp(-\psi^*/kT)/\exp(-\psi/kT) = \exp[-(\psi^* - \psi)/kT]$, where ψ and ψ^* respectively are the energies of interaction of the normal and the activated ion with its solvent neighbours. If c and c^* denote the corresponding co-ordination numbers, and D the energy required to remove one solvent molecule to infinity from its equilibrium position around the ion, then n^*/n is proportional to $\exp[-(c - c^*)D/kT]$. A similar expression holds for the ratio of the concentration of partly de-solvated solute molecules to the total concentration. The rate of reaction is $dn/dt = Zn^*_1n^*_2 = Zn_1n_2 \exp\{-[(c_1 - c_1^*)D_1 + (c_2 - c_2^*)D_2]/kT\}$, where Z is proportional to the collision frequency (and is not to be confused with kT/h or any other frequency term which may be applicable to unimolecular reactions). The bimolecular velocity coefficient is then $k_2 = (dn/dt)/n_1n_2 = Z\{\exp - [(c_1 - c_1^*)D_1 + (c_2 - c_2^*)D_2]/kT\}$ and, details being omitted, the true energy of activation, E, becomes

$$E = (c_1 - c^*_1)D_1 + (c_2 - c^*_2)D_2$$

The energy required to deprive an ion of one of its sheath molecules is E_s/c_1, where E_s is the gain in energy when the ion is removed from solution. The values adopted for E_s, in kcals./g.-ion, are 98·6 (F), 66·9 (Cl^-), 58·1 (Br^-), 48·9 (I^-), and 84·4 (OH^-). They have been obtained from recent data published by the National Bureau of Standards,[23] supplemented by the electron affinity of the hydroxyl ion given by Page.[24] We shall assume that only one molecule of solvent need be removed from the sheath about the solute molecule, *i.e.* that $c_2 - c^*_2 = 1$. Then

$$E_1 = E_s(c_1 - c_1^*)/c_1$$

Following Glew and Moelwyn-Hughes,[4] it has been assumed that c^*_1 is 4 when c_1 is 6, and 3

[21] Hinshelwood, "The Kinetics of Chemical Change in Gaseous Systems," Oxford, 1933, pp. 233—241.
[22] Moelwyn-Hughes, "The Kinetics of Reactions in Solution," Oxford, 1933, pp. 51—73.
[23] National Bureau of Standards Circular 500, Washington D.C., 1952.
[24] Page, *Discuss. Faraday Soc.*, 1955, **19**, 87.

XUM

when c_1 is 4. The energy term D_2 can be estimated [4] from the dipole moments of the solute and solvent molecules and the dielectric constant of the solvent:

$$D_2 = 2\left[\mu_1\mu_2\left(\frac{D+2}{9D}\right)\right]^2 \cdot A^{-1}$$

where $A = 1{\cdot}66 \times 10^{-32}$ erg. cm.[9] Table 12 gives a comparison of observed energies of activation (E_A), in kcal./mole, with those calculated in this way.

DEPARTMENT OF PHYSICAL CHEMISTRY, CAMBRIDGE. [*Received, October 30th*, 1958.]

---

531. *Effects of γ-Radiation. Part I. Polymer Formation * from Sugars, Hydroxy-acids, and Amino-acids.*

By S. A. BARKER, P. M. GRANT, M. STACEY, and R. B. WARD.

Acidic polymers have been formed by γ-irradiation of aqueous solutions of maltose, glucose, 1 : 4-gluconolactone, lactic acid, glycollic acid, and amino-acid solutions *in vacuo*. The isolation and initial structural investigations of some of these unusual polymers are described.

PROLONGED irradiation of aqueous glucose solutions (0·1%) *in vacuo* from a 200 c ^{60}Co source has been found to lead to an acidic polymer.[1] Irradiated solutions were freeze-dried since the ultraviolet absorption spectrum of the aqueous polymer solution changed slowly at 20° and rapidly at 100° (Fig. 1). This change was not reversed on subsequent freeze-drying, and did not appear to be associated with an appreciable change in molecular size. Dialysis was, in some ways, not an ideal technique for the isolation of the polymer since the pore-size of the membrane varied, and some material was not of a sufficiently high molecular weight to be retained. Cetavlon [2] (cetyltrimethylammonium bromide) precipitated more polymer from the dialysate, presumably of a lower molecular weight. M-Sodium chloride, added to an ethanolic solution of the polymer–Cetavlon complex, precipitated a material having the same infrared and ultraviolet absorption spectra and identical chromatographic and ionophoretic properties as the polymer initially obtained by dialysis.

The yields of polymeric material recovered by dialysis of a number of γ-irradiated solutions of glucose, maltose, 1 : 4-gluconolactone, lactic acid, and glycollic acid are shown in Table 1. Carbon dioxide was evolved in each case during the irradiations. In the case of glycollic acid, the low yields were increased by further irradiation.

TABLE 1. *Yields of polymers.*

			Yields (%)	
Ref. No.	Substrate	Dose ($\times 10^{20}$ ev ml.$^{-1}$)	Non-volatile	Polymer (non-diffusible)
1	Maltose	4·44	83	1·4
2	Glucose	1·46	75	1·3
3	Glucose	4·44	62	45
4	1 : 4-Gluconolactone	4·54	68	51
5	Lactic acid	4·54	40	4·8
6	Glycollic acid	4·54	39	4·5
7	,,	0·91	85	0
8	,,	4·3	42	2·2
9	,, *	9·2	36	6·4
10	Mandelic acid	4·3	68	61 †

* 0·15%, otherwise 0·1%. † Yield of precipitate; no dialysis in this case.

The polymers show considerable similarity, apart from the special case of mandelic acid (see below). Elemental analyses showed, *e.g.*, the polymer no. 4 to be approximately

* Patent Appln., 698/59.

[1] Barker, Grant, Stacey, and Ward, *Nature*, 1959, **183**, 376.

[2] Jones, *Biochim. Biophys. Acta*, 1953, **10**, 607; Bera, Foster, and Stacey, *J.*, 1955, 3788.

TABLE 2. *Properties of polymers.*

Ref. no.	Polymer Parent substance	Found (%) C	H	Ionophoresis M_G	$M_{Gluconic}$	"Apparent CHO" (%)	Acid-labile CO_2 (%)	Equiv. at pH 7	pH 9
1	Maltose	—	—	0·7—1·0	0·2—1·0	—	—	—	—
2	Glucose	43·99	4·61	—	—	—	—	—	—
3	Glucose	51·91	5·07	1·1	1·25	16·0	4·2	450	328
4	1 : 4-Gluconolactone	50·37	5·40	1·1	1·25	16·8	2·2	408	322
5	Lactic acid	52·21	6·32	1·1	1·22	7·8	—	—	—
8	Glycollic acid	50·46	5·25	1·1	1·32	12·0	7·7	196	165
9	Glycollic acid	52·14	4·75	1·1	1·32	10·4	—	249	196
10	Mandelic acid (ppt.)	70·04	6·10	—	—	—	—	—	—

TABLE 3. *Infrared absorption bands (cm.$^{-1}$).*

Polymers					Acid-hydrolysis of glycollic acid polymer (no. 9)		Mandelic acid
Maltose 1	Glucose 3	1 : 4-Glucono-lactone 4	Lactic acid 5	Glycollic acid 8, 9	Ppt.	Sol.	ppt. (no. 10)
3350s	3400s	3350s	3350s	3400s	3400s	3400s	3400s
2900w	2910w	2950w	2950w	2950w	2950w	2950w	2940m
					2600w	2600m	
2350w	2350w	2350w		2350w			
2170w	2170w	2130w	2100w	2100w		2050w	
						1925m	
1710m	1710w	1710w	1710w	1780m	1725s		
			1650s			1650s	1680s
1600m	1590s	1600s			1635m		1620w
					1525w		1510m
			1460w				1470m
1405w	1415s	1410s	1410m	1410m	1400w	1360s	
					1200m		1250b
			1130w			1125w	
1020s	1090m	1090m	1110w		1100m	1050w	
			1050w			1035w	1040mb
						1000m	930w
						835s	770m
						700s	710s

$(C_6H_8O_4)_n$ (Table 2). The polymers were immobile during chromatography in butan-1-ol–ethanol–water (4 : 1 : 5 v/v) or butan-1-ol–propionic acid–water (6 : 3 : 4 v/v) and were detected by alkaline silver nitrate [3] or Chlorophenol Red.[4] On ionophoresis in 0·2M-borate buffer (pH 10), the polymers had M_G ~1·1 and in 0·2M-acetate buffer (pH 5) had $M_{Gluconic\ acid}$ 1·2—1·3.

All the polymers were precipitated from solution by Cetavlon,[2] the precipitate being soluble in M-sodium chloride. The polymers were also precipitated by cold dilute acid, the precipitates having infrared spectra identical with those of the original polymers (Table 3). These precipitates (contrast the hot acid-hydrolysis below) were readily soluble in cold dilute ammonia solution.

The infrared absorption spectra of these polymers were similar (Table 3). The ultra-violet absorption spectra show peaks in the region 260—270 mμ which were less pronounced in the spectra of the polymers from lactic and glycollic acid (Fig. 1).

Treatment of the polymers from glucose (no. 3 *) and glycollic acid (no. 9) with hot dilute acid formed precipitates (in 61% and 41% yield respectively) having infrared absorption spectra similar to those of the original polymers. The precipitates were insoluble in aqueous ammonia and sodium hydroxide. The soluble fractions from the acid-treatments were examined by paper chromatography. The soluble fraction from the glucose polymer contained no detectable mobile components, but the soluble fraction from the glycollic acid polymer contained at least two unidentified non-reducing components.

* Such numbers refer to Table 1.

[3] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.

[4] Block, Durrum, and Zweig, "A Manual of Paper Chromatography and Paper Electrophoresis," Academic Press, Inc., New York, 1955, p. 169.

XUM

The polymers are oxidised by alkaline hypoiodite. The method of Hirst, Hough, and Jones [5] was used to measure the " apparent aldehyde " group content (Table 2).

The polymers from glucose (no. 3) and glycollic acid (nos. 8 and 9) were oxidised with periodate.[6] All showed a rapid uptake followed by a slower reaction; increased dosage of radiation yielded a polymer which was attacked more slowly (Fig. 2). At the end of the periodate oxidation, the reaction mixtures yielded non-diffusible materials. The periodate-oxidised polymers thus obtained had infrared absorption spectra very similar to those of the parent polymers. Alkaline hypoiodite oxidation [5] of the periodate-oxidised glycollic acid polymer (no. 9) showed 5·8% of " apparent aldehyde " group, approximately half the value obtained before periodate oxidation.

Similarly alkaline hypoiodite oxidation [5] of the polymer from glycollic acid (no. 9) yielded non-diffusible materials (84%), and the periodate-oxidised glycollic acid polymer

FIG. 1.

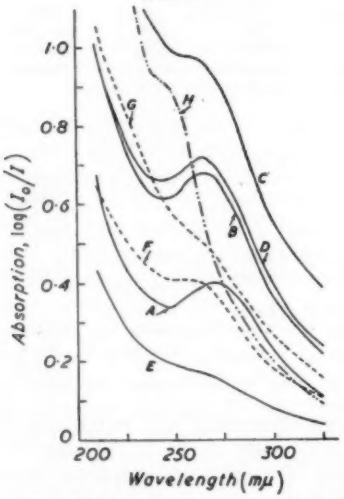


FIG. 2.

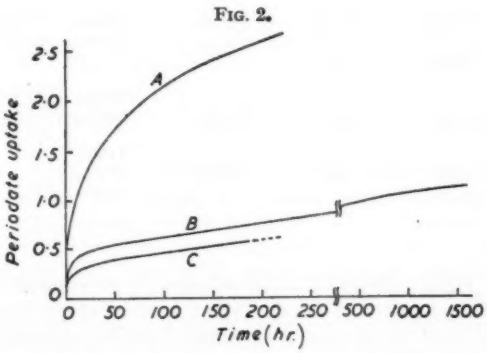


FIG. 1. *Ultraviolet absorption spectra of polymers. Polymers from (A) maltose (no. 1 in Table 1), (B) glucose (no. 3), (C) glucose (no. 3) after being heated at 100° for 10 min., (D) 1 : 4-gluconolactone (no. 4), (E) lactic acid (no. 5), (F) glycollic acid (no. 9), (G) periodate-oxidised glycollic acid polymer (no. 9), (H) mandelic acid precipitate (no. 10). A—G, 0·1% solutions in water. H, 0·05% solutions in ethanol.*

FIG. 2. *Oxidation of polymers by periodate. (A) Glucose polymer (no. 3). (B) Glycollic acid polymer (no. 8). (C) Glycollic acid polymer (no. 9). Periodate uptake is plotted in mmole per 180 mg. for (A), and in mmole per 76 mg. for (B) and (C).*

(no. 9) when oxidised with alkaline hypoiodite yielded 90% of non-diffusible material. All the hypiodite-oxidised polymers had infrared absorption spectra very similar to those of the original polymers.

The acidimetric equivalent was determined by potentiometric titrations (Table 2). The carbon dioxide evolved when the materials were heated with 19% hydrochloric acid was determined as a measure of ready decarboxylation [7] (Table 2).

1 : 4-Gluconolactone was irradiated in 99·78% deuterium oxide solution. The infrared absorption spectra of the non-volatile solute and polymer showed no indication of carbon–deuterium bond formation, indicating that virtually no carbon–hydrogen bonds underwent hydrogen exchange with the solvent or radicals derived therefrom.

[5] Hirst, Hough, and Jones, *J.*, 1949, 928.
[6] Dyer, " Methods of Biochemical Analysis," Interscience Publ., Inc., New York, 1956, Vol. III, p. 111.
[7] Barker, Foster, Siddiqui, and Stacey, *Talanta*, 1958, **1**, 216.

Glycine, alanine, and phenylalanine solutions on irradiation also yielded materials which were precipitated by Cetavlon, the complex being soluble in M-sodium chloride. The isolation of polymeric material by dialysis has not yet been attempted in these cases.

The presence of oxygen was found completely to inhibit polymer formation in all cases, but polymer formation ensued when the irradiation occurred under a stream of nitrogen.

Discussion.—The polymers formed are acidic and are susceptible to both alkaline hypoiodite [5] and periodate [6] oxidation, but in neither oxidation is the polymeric character destroyed. The polymeric character, furthermore, survives acidic and alkaline hydrolysis, although superficial degradation occurs, *e.g.*, partial decarboxylation and slight fragmentation. This emphasises that the linkage is neither glycosidic nor that of an ester. Infrared spectroscopy reveals that the lactic acid polymer (no. 5) and mandelic acid precipitate (no. 10) retain some of the methyl and phenyl groups respectively, while the formation of small amounts of glucose on hydrolysis of the maltose polymer (no. 1) shows that some of the *O*-glucosyl substituent also survives. When the parent molecule contains phenyl groups, it might be expected that polymerisation would markedly decrease solubility. This is evident with the slightly soluble phenylalanine product and in the precipitation in the case of mandelic acid. Once precipitated, further attack will be slower, since attack by solvent radicals then becomes heterogeneous.

It has been shown [8] that the direct action of γ-radiation on polycrystalline glycollic acid *in vacuo* forms carboxyhydroxymethyl radicals. Tartaric acid has been shown to be a relatively stable primary product formed in high yield on irradiation of aqueous glycollic acid *in vacuo*,[9] and solutions both of tartaric acid and of mixtures of tartaric and glycollic acid [1] give acidic products of larger molecular size *in vacuo*. It is postulated, therefore, that the polymers are formed by such radical addition. In the case of glycollic acid, this would be expected to yield a polymeric repeating unit: $[-C(CO_2H)(OH)-]$. However, the growing molecule would be subject to further attack at alternative sites (as observed with the simpler molecules [1,9]). Comparison of the properties of the polymers (nos. 8 and 9) from glycollic acid, which have been formed after mean molecular doses of 55 and 78 ev/molecule respectively, showed lower carboxylic acid and aldehyde contents and greater resistance to attack by periodate with increasing dose. The last-mentioned effect is of particular importance since the hypothetical repeating unit above would be sensitive to periodate cleavage. It appears (Fig. 2) that further radiation is mainly affecting such structures as would be rapidly oxidised by periodate. Formation and destruction of aldehyde groups may be expected in a manner similar to the formation of glyoxylic acid from glycollic acid and its destruction.[9]

The main route for polymer formation from glucose is believed to be through gluconic acid. The evidence for this lies in the high yield of gluconic acid from glucose solutions irradiated *in vacuo*,[10] the increased yield of polymer from 1 : 4-gluconolactone, and the strong similarity between the polymers from glucose (no. 3) and from 1 : 4-gluconolactone (no. 4). Similar mechanisms are therefore believed to account for the polymer formation in each case. This is supported by the use of electron-spin resonance techniques to detect, *inter alia*, the aminocarboxymethyl radical $[\cdot CH(NH_3^+)\cdot CO_2^-]$ in irradiated crystalline glycine *in vacuo* [11] and the detection of apparent amino-acid dimers by chromatography of irradiated solutions of amino-acids.[1] Such mechanisms would produce polymer yields very dependent on the molecular size of the initial compound, and, with the exception of the polymer from maltose (no. 1), this is indicated in Table 1.

It is pertinent to notice that the presence of oxygen inhibits polymer formation and also formation of tartaric acid from glycollic acid [9] and of larger molecules from a number

[8] Grant, Ward, and Whiffen, *J.*, 1958, 4635.
[9] Grant and Ward, following papers.
[10] Grant and Ward, *J.*, in the press.
[11] Ghosh and Whiffen, *Chem. Soc. Spec. Publ.* No. 12, 1958, p. 168.

XUM

of relevant compounds in aqueous solution.[1] It is just such radical addition which would be prevented by rapid formation of peroxy-radicals in the presence of oxygen.

These investigations, which are being continued, have given evidence for carbon–carbon addition to form polymeric materials. The parts of the initial molecules not involved in addition undergo concurrent radiative degradation to yield carbonyl groups, carboxylic acid groups, and other chemical species, which are chemically labile in contrast to the inert polymeric linkage.

Experimental

The polymers are described by reference numbers, as given in Table 1.

Polymer Preparation.—An aqueous solution (0·1% or exceptionally 0·15%) of the compound was boiled vigorously under a vacuum at room temperature for 2 hr. and sealed. The stirred solution was irradiated from a 200 c ^{60}Co γ-radiation source [12] (dose rate $14{\cdot}2 \times 10^{16}$ ev min.$^{-1}$ ml.$^{-1}$ for polymers nos. 4, 5, and 6; otherwise $3{\cdot}8 \times 10^{16}$ ev min.$^{-1}$ ml.$^{-1}$), and then freeze-dried. The residue was weighed, dissolved in water to give a 10% solution, and dialysed for 4 days against 25 vol. of distilled water which was changed daily. The non-diffusible material was recovered by freeze-drying. The parent substances were all free of non-diffusible materials before irradiation. Mandelic acid (4 g.), on irradiation as above, gave a white precipitate (no. 10) (2·43 g.), and the supernatant liquid on freeze-drying yielded 0·27 g. of a pale yellow solid.

Properties of the Polymers.—(i) *Chromatography and ionophoresis.* Chromatography with butan-1-ol–ethanol–water (4 : 1 : 5 v/v) or butan-1-ol–propionic acid–water (6 : 3 : 4 v/v) showed a single immobile component in each polymer, detectable with alkaline silver nitrate [3] and Chlorophenol Red,[4] but only faintly with aniline hydrogen phthalate.[13] Ionophoresis in 0·2M-borate buffer (pH 10) and 0·2M-acetate buffer (pH 5) showed similar mobilities for all the polymers (Table 2).

(ii) *Precipitation with Cetavlon.* Each polymer was precipitated from solution by the addition of 2% aqueous Cetavlon (cetyltrimethylammonium bromide) solution. Cetavlon also gave a slight precipitate from the concentrated dialysable fraction. The precipitates redissolved in M-sodium chloride. A portion of the Cetavlon complex was washed with water, dissolved in ethanol, and treated with M-sodium chloride, a precipitate being formed whose ultraviolet and infrared spectra and analysis were identical with those of the polymer obtained by dialysis.

(iii) *Infrared and ultraviolet absorption spectra.* Infrared spectra are shown in Table 3, and the ultraviolet spectra in Figure 1.

(iv) *Periodate oxidation.*[6] Glucose polymer (no. 3) (84·01 mg.) was oxidised with 0·15M-sodium metaperiodate (50 ml.). Glycollic acid polymers (no. 8) (15·48 mg.) and (no. 9) (30·0 g.) were oxidised with 0·05M-sodium metaperiodate (25 and 50 ml. respectively). The uptake of oxidant at room temperature in the three cases is shown in Fig. 2. The formaldehyde and acid content in the reaction mixtures was determined colorimetrically with chromotropic acid [6,14] and titrimetrically with sodium hydroxide [6] respectively after 72 hr. The values obtained for the glucose polymer (no. 3) were 0·0012 mmole of formaldehyde and 0·41 milliequiv. of acid per 180 mg. of polymer. Glycollic acid polymer (no. 8) yielded 0·019 mmole of formaldehyde and 0·316 milliequiv. of acid per 76 mg. of polymer. Glucose polymer (no. 3) (30 mg.) was oxidised at room temperature with 0·15M-sodium metaperiodate (10 ml.). After 100 hr. the excess of periodate was destroyed with ethylene glycol, and the solution dialysed for 4 days as described for the preparation of the polymers. The non-diffusible fraction yielded 10 mg. on freeze-drying. This periodate-oxidised polymer had very similar chromatographic properties and infrared absorption spectrum to its parent glucose polymer (no. 3), and gave with 2% Cetavlon solution a precipitate which was soluble in M-sodium chloride. Ionophoresis showed a single component with M_G 1·1 and $M_{\text{Gluconic acid}}$ 1·25.

Similarly glycollic acid polymer (no. 9) (270 mg.) was oxidised with 0·05M-sodium metaperiodate (450 ml.). The reaction was stopped with ethylene glycol after 160 hr. and the solution dialysed as before. The non-diffusible fraction yielded 144 mg. (Found: C, 45·1; H, 4·0; Ash, 8·0%). Again the periodate-oxidised polymer was indistinguishable from its parent

[12] Gibson and Pearce, *Chem. and Ind.*, 1957, 613.
[13] Partridge, *Nature*, 1949, **164**, 443.
[14] MacFadyen, *J. Biol. Chem.*, 1945, **158**, 107.

XUM

glycollic acid polymer by means of its infrared absorption spectrum, chromatographic properties, or behaviour with 2% Cetavlon solution. Ionophoresis showed a single component with M_G 1·1—1·2 and $M_{Gluconic\ acid}$ 1·4—1·6. The ultraviolet absorption spectrum showed much less indication of a point of inflexion in the region 250—270 mμ than for the parent polymer.

(v) *Alkaline-hypoiodite oxidation.* The polymers were oxidised as described by Hirst, Hough, and Jones,[5] the reagents being calibrated with glucose (Table 2). The results are expressed as aldehyde content (%).

Additionally the periodate-oxidised polymers obtained from glucose and glycollic acid (see iv above) were oxidised with alkaline hypoiodite, and had " apparent aldehyde " contents of 1·0 and 5·8% respectively.

The polymer from glycollic acid (no. 9) (100 mg.) and periodate-oxidised glycollic acid polymer (30 mg.) were separately oxidised with alkaline hypoiodite. The solutions were neutralised with hydrochloric acid, freeze-dried, dissolved in a small volume of water, and dialysed as described for the preparation of the polymers. The non-dialysable fractions yielded 84 and 24 mg. respectively on freeze-drying. These solid oxidised polymers both gave precipitates with 2% Cetavlon solution, and the precipitates were soluble in M-sodium chloride. The infrared spectra were both very similar to that of the parent glycollic acid polymer (no. 9).

(vi) *Potentiometric titration.* The polymers were titrated with 0·0503N-sodium hydroxide in an atmosphere of nitrogen. The equivalent of the polymer was calculated on the basis of the alkali required to establish stable pH values of 7·0 and 9·0. These equivalent values are shown in Table 2.

(vii) *Acidic hydrolysis.* Maltose polymer (no. 1) (1·2 mg.) was hydrolysed for 5 hr. at 100° with 1·5N-sulphuric acid (5 ml.). The solution darkened and a brown precipitate was formed. After neutralisation of the solution with barium carbonate, glucose was detected by paper chromatography and ionophoresis as the only mobile component.

Glucose polymer (no. 3) (50·4 mg.) was dissolved in water (2 ml.), and 2N-sulphuric acid (6 ml.) was added. The immediate white precipitate dissolved at 100° in 4 hr., while the solution became darker and an insoluble material (30·7 mg.) was obtained (Found: C, 56·6; H, 5·1; ash, 0·5%). The material was insoluble in water, 2N-ammonia, acetone, or ethanol, but was slowly soluble in hot N-sodium hydroxide, from which it was precipitated by the addition of acid. The infrared spectrum of this material showed peaks at 3400s, 2950w, 1730w, 1640w, 1180s, 1070w, 1010w, and three weak peaks between 890 and 950 cm.$^{-1}$ (cf. Table 3).

The solution obtained by hydrolysis was neutralised with barium carbonate and filtered. No mobile components were detected in the filtrate on chromatographic analysis.

Glycollic acid polymer (no. 9) (100·4 mg.) was heated with 2N-sulphuric acid (20 ml.) for 3 hr. at 100°. A brown precipitate (infrared spectrum, Table 3) was formed (41 mg.) (Found: C, 51·7; H, 4·2; ash, 3·1%). The supernatant liquid was neutralised with barium carbonate, filtered, and freeze-dried to a pale brown powder (23·6 mg.; for the infrared spectrum see Table 3). Ionophoresis in 0·2M-borate buffer (pH 10) showed components with M_G values of 0·9 and 1·0; but on ionophoresis in 0·2M-acetate buffer (pH 5) no mobile components were detected. Chromatography in butanol–propionic acid–water showed components with $R_{Glyoxylic\ acid}$ 0·13 and 0·25, and a streaking, faster component; with butanol–ethanol–water components with $R_{Glyoxylic\ acid}$ 0·40 and 0·70 and a streaking, slower component were detected. The components were detected by alkaline silver nitrate but not by aniline hydrogen phthalate. Oxidation by alkaline hypoiodite showed this soluble fraction to have an " apparent aldehyde " content of only 0·8%.

(viii) *Evolution of carbon dioxide on treatment with acid.*[7] The polymers were heated in 19% hydrochloric acid. The carbon dioxide evolved was swept with nitrogen into alkali and determined titrimetrically. The carbon dioxide evolved is shown in Table 2.

(ix) *Alkaline hydrolysis.* Glycollic acid polymer (no. 8) (2 mg.) was heated at 100° for 2 hr. with 2N-barium hydroxide (2 ml.). An insoluble brown material was formed and was filtered off. The solution was neutralised with carbon dioxide, filtered, and freeze-dried twice to remove barium hydrogen carbonate. Paper chromatography and ionophoresis revealed soluble products similar to those obtained by acidic hydrolysis of the polymer.

(x) *Degradation of the glucose polymer in solution.* The ultraviolet absorption spectrum of the polymer from glucose (no. 3) changed in aqueous solution slowly at 20° and rapidly at 100°. Freeze-dried solutions had unchanged ultraviolet absorption spectra (Fig. 1).

XUM

Special Preparation of Polymers.—(i) *In deuterium oxide.* Dried 1 : 4-D-gluconolactone (20 mg.) was dissolved in deuterium oxide (20 ml.; 99·78% of D_2O) and irradiated as for polymer (no. 4) *in vacuo* in the absence of water. The solution was then freeze-dried. The non-volatile solute and the non-diffusible fraction were examined by infrared spectroscopy, but yielded no evidence of carbon–deuterium bond formation.

(ii) *Attempted preparation of glucose polymer in the presence of oxygen.* 0·1% Glucose solution (4 l.) was degassed and saturated with oxygen for 2 hr. The solution was irradiated for 8 days (dose rate $3{\cdot}8 \times 10^{16}$ ev min.$^{-1}$ ml.$^{-1}$, total $4{\cdot}4 \times 10^{20}$ ev ml.$^{-1}$) in the presence of a continuous stream of oxygen. The freeze-dried solution gave no precipitate with 2% Cetavlon solution and yielded no non-diffusible material.

(iii) *Preparation of glucose polymer in the presence of nitrogen.* The previous experiment was repeated with a nitrogen stream in place of oxygen. The freeze-dried solution gave a copious precipitate with 2% aqueous Cetavlon and yielded non-diffusible material as *in vacuo*.

Polymer Formation from Amino-acids.—0·1% Aqueous solutions (20 ml.) of glycine, alanine, and phenylalanine were irradiated *in vacuo* and in the presence of oxygen for 3 days (dose rate $14{\cdot}2 \times 10^{16}$ ev min.$^{-1}$ ml.$^{-1}$, total $6{\cdot}1 \times 10^{20}$ ev ml.$^{-1}$). No precipitation occurred when 2% Cetavlon solution was added to the oxygenated solutions, but the three amino-acid solutions irradiated *in vacuo* gave large precipitates. The freeze-dried non-volatile solutes from the evacuated systems were readily soluble in water, with the exception of the phenylalanine polymer which was soluble only to the extent of *ca.* 2 mg./ml. [cf. mandelic acid precipitate (no. 10)].

The authors thank the United Kingdom Atomic Energy Authority, Research Division, Harwell, for support of this investigation, and for maintenance grants to P. M. G. and R. B. W.

THE CHEMISTRY DEPARTMENT,
THE UNIVERSITY, BIRMINGHAM, 15. [*Received, January 15th*, 1959.]

---

532. *Effects of γ-Radiation. Part II.*[1] *Characterisation of the Products from Glycollic Acid.*

By P. M. GRANT and R. B. WARD.

The non-volatile products formed by γ-irradiation of glycollic acid solutions *in vacuo* have been isolated and identified as glyoxylic, oxalic, and tartaric acid. They are explained by formation and reactions of the carboxyhydroxymethyl radical, $\cdot CH(OH)\cdot CO_2H$. The effect of oxygen on the reactions of the radical is discussed. Preliminary studies of the effect of γ-radiation on the products have been made.

PRELIMINARY chromatographic and ionophoretic studies of glycollic acid solutions which had been irradiated *in vacuo* showed the formation of glyoxylic (characteristic yellow colour with aniline hydrogen phthalate [2]), tartaric, and oxalic acid, and prompted a more detailed study. In the present work, the initial glycollic acid concentration was 0·1% (0·0132M), and the dose-rate $3{\cdot}8 \times 10^{16}$ ev min.$^{-1}$ ml.$^{-1}$ (determined by the ferrous ammonium sulphate actinometer [3]) by which, in 24 hr., approximately a quarter of the glycollic acid had been degraded. After irradiation for 24 hr. under these conditions *in vacuo*, the solutions contained essentially glycollic, glyoxylic, tartaric, and oxalic acid, but at least three other minor components were detected which were believed to be compounds akin to dihydroxytartaric acid and further radical-addition products from tartaric and glycollic acid. Much longer irradiation gives [1] considerable quantities of non-diffusible polymeric materials, and some such polymer is therefore to be expected after 24 hr.; however, after 12 hr. only glycollic, glyoxylic, tartaric, and oxalic acid could be detected.

After irradiation for 24 hr. *in vacuo*, glycollic and oxalic acid were isolated as such

[1] Part I, Barker, Grant, Ward, and Stacey, preceding paper.
[2] Partridge, *Nature*, 1949, **164**, 443.
[3] Hardwick, *Canad. J. Chem.*, 1952, **30**, 17; Donaldson and Miller, *J. Chim. phys.*, 1955, **52**, 578.

XUM

(characterised as *S*-benzylthiuronium salts), glyoxylic acid as its 2:4-dinitrophenylhydrazone, and tartaric acid as its *p*-nitrobenzyl ester.

The mechanism of formation of these compounds is probably as follows,[4] hydrogen abstraction being by the radicals directly formed from the solvent:

$$H_2O \rightsquigarrow H\cdot + \cdot OH$$

$$HO\cdot CH_2\cdot CO_2H \xrightarrow[-H]{} \cdot CH(OH)\cdot CO_2H$$

$$2\cdot CH(OH)\cdot CO_2H \longrightarrow HO_2C\cdot CH(OH)\cdot CH(OH)\cdot CO_2H$$

$$\cdot CH(OH)\cdot CO_2H \xrightarrow[\cdot OH]{} (HO)_2CH\cdot CO_2H \,[\longrightarrow CHO\cdot CO_2H + H_2O]$$

$$(HO)_2CH\cdot CO_2H \xrightarrow[-H]{} \cdot C(OH)_2\cdot CO_2H$$

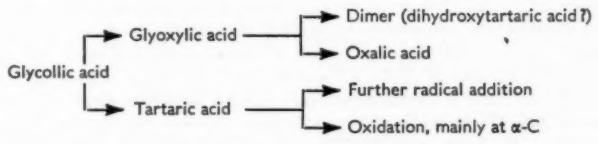
$$\cdot C(OH)_2\cdot CO_2H \xrightarrow[\cdot OH]{} (HO)_3C\cdot CO_2H \,[\longrightarrow HO_2C\cdot CO_2H + H_2O]$$

Dehydrogenation of glycollic acid by radicals from the solvent may be expected because of the activation of the α-hydrogen atom by the carboxyl group. In fact, the direct effect of γ-radiation on polycrystalline glycollic acid *in vacuo* results in almost exclusive formation of the carboxyhydroxymethyl radical,[5] and detection of this radical by its electron spin resonance spectrum shows the readiness with which the process occurs. Subsequent work[6] has shown that the rates of formation of glyoxylic and tartaric acid are those expected for primary products, and that of oxalic acid is as expected for a later product.

Brief chromatographic and ionophoretic studies have been made of the γ-irradiation of solutions of glyoxylic, tartaric, and oxalic acid *in vacuo*. Glyoxylic acid yielded oxalic acid, but also at least two other acidic compounds which had R_T (*i.e.*, *R* relative to tartaric acid) 1·0 and 0·6, corresponding to C_4 and C_6 molecules. Ionophoretic mobilities showed the equivalent weight to remain approximately constant, suggesting the formation of a dibasic "dimer" and a tribasic "trimer." These products reduced aniline hydrogen phthalate,[1] and the former behaves similarly to dihydroxytartaric acid which would be the expected product if condensation of two carboxydihydroxymethyl radicals $\cdot C(OH)_2\cdot CO_2H$ had occurred.

Oxalic acid yielded only traces of non-volatile products, mainly one component having R_T 0·6, which suggests that under certain circumstances reductive coupling can occur.

Tartaric acid produced only a small amount of one faster-moving component, tentatively postulated as a C_3 aldehyde. This component was non-acidic and in mobility equalled mesoxalic acid. Aniline hydrogen phthalate disclosed this component and differentiated it by its colour (brown) from mesoxalic acid (yellow). The main component from tartaric acid was acidic and had R_T 0·3 and the ionophoretic mobility expected for a C_8 tetrabasic dimer. Also, on chromatography, components in the tartaric acid region became detectable with aniline hydrogen phthalate, suggesting some oxidation of the tartaric acid without C–C scission. No glyoxylic or glycollic acid, however, could be detected in the products from tartaric acid. These observations are compatible with the above mechanism, which may be extended, thus:



[4] Cf. Johnson, Scholes, and Weiss, *J.*, 1953, 3091; Hart, *Radiation Res.*, 1954, **1**, 53; Garrison, Haymond, and Weeks, *ibid.*, p. 97.
[5] Grant, Ward, and Whiffen, *J.*, 1958, 4635.
[6] Grant and Ward, Part III, following paper.

XUM

We next studied degradation by γ-radiation of aqueous glycollic acid solutions continuously aerated with oxygen. Glyoxylic and oxalic acid were found as before, and in higher yields, with tartaric acid in very much smaller quantities.

It appears unlikely that the initial abstraction of hydrogen would be modified by the presence of oxygen, but the oxygen would readily yield peroxy-radicals from organic radicals once these had been formed:

$$HO{\cdot}CH_2{\cdot}CO_2H \xrightarrow[-H]{} {\cdot}CH(OH){\cdot}CO_2H \xrightarrow[O_2]{} {\cdot}O{\cdot}O{\cdot}CH(OH){\cdot}CO_2H$$

$$2\,{\cdot}O{\cdot}O{\cdot}CH(OH){\cdot}CO_2H + 2\,{\cdot}HO_2 \longrightarrow 2\,CHO{\cdot}CO_2H + H_2O_2 + O_2$$

Many workers [4] have established this type of reaction and shown that such peroxy-radicals react, almost exclusively, to yield a molecule where, ultimately, a hydroxyl group is substituted on the peroxy-radical site, in this case yielding glyoxylic acid. The reaction of the initial radical with oxygen would thus much reduce the formation of tartaric acid, since the life of the peroxy-radical is likely to be much longer than that of the parent radical in the presence of excess of oxygen.

This concept is substantiated by observations on the irradiation of glyoxylic, oxalic, and tartaric acid separately in the presence of oxygen, where the formation of components by C–C linkage virtually ceased. Glyoxylic acid appeared to yield solely oxalic acid, which, in turn, yielded no detectable non-volatile products. Tartaric acid, also, showed no components with $R_T < 1$, but there was more formation of compounds sensitive to aniline hydrogen phthalate in the tartaric acid region than there was *in vacuo*, also of components behaving as mesoxalic acid and glyoxylic acid (the latter in traces).

The reaction of the radicals with oxygen, giving ultimately glyoxylic acid, explains why polymers are not formed in such cases: for it is addition of these radicals to one another that is believed to cause polymer formation from, *e.g.*, glycollic acid *in vacuo*.[1,7]

It should be emphasised that both in the presence and in the absence of oxygen some degradation occurs to volatile products such as formaldehyde, formic acid, and carbon dioxide. This aspect is considered elsewhere.[6]

Experimental

Irradiation Procedure.—Solutions were placed round a 200 c ^{60}Co γ-radiation source similar to that described by Gibson and Pearce.[8] The solutions were stirred continuously during irradiation. The dose-rate throughout was $3{\cdot}8 \times 10^{16}$ ev. min.$^{-1}$ ml.$^{-1}$, determined by the ferrous ammonium sulphate actinometer, [$G(Fe^{++} \longrightarrow Fe^{+++}) = 15{\cdot}6$].[3] The volume irradiated was 4 l. Alternatively smaller volumes in units of 20 ml. were irradiated at a dose-rate of $14{\cdot}2 \times 10^{16}$ ev min.$^{-1}$ ml.$^{-1}$.

Identification of the Products formed by Irradiation of Glycollic Acid in vacuo.—(i) *Fractionation of the non-volatile solute.* A solution of glycollic acid (4 g.) in water (4 l.) was boiled *in vacuo* for 2 hr. with frequent shaking. The vessel was sealed under a vacuum and irradiated for 24 hr. (total dose, $5{\cdot}5 \times 10^{19}$ ev ml.$^{-1}$) with gentle stirring. The solution was then freeze-dried [9] and the solid (*ca.* 4·1 g.) dissolved in water (100 ml.) and neutralised with excess of calcium carbonate with vigorous stirring. The precipitates A″ (immediate) and B″ (after 48 hr.) were removed. The filtrate was freeze-dried, dissolved in water, filtered from calcium carbonate, concentrated, and allowed to crystallise repeatedly, to give crystals (C′) and mother-liquor, which was freeze-dried (D′). A″ and B″ were extracted with cold 2N-acetic acid to yield residues A′ (0·27 g.) and B′ (0·74 g.) and extracts E′ and F′ respectively.

Fractions C′, D′, E′, and F′ were separately passed in dilute aqueous solution through an excess of Zeo-Karb 225 (H^+ form) to remove calcium. Freeze-drying the eluates gave materials C (3·5 g.), D (0·25 g.), E (7 mg.) and F (12 mg.). A′ and B′ were treated with an insufficiency of 2N-sulphuric acid, stirred, and filtered, yielding solutions A and B, which were freeze-dried.

[7] Barker, Grant, Ward, and Stacey, *Nature*, 1959, **183**, 376.
[8] Gibson and Pearce, *Chem. and Ind.*, 1957, 613.
[9] Grant and Ward, *J. Sci. Instr.*, 1959, **36**, 133.

XUM

(ii) *Chromatography and ionophoresis of fractions A—D.* Each fraction was analysed by chromatography in propionic acid–butan-1-ol–water (6 : 3 : 4 v/v) and ionophoresis in 0·75M-formate buffer (pH 2·0) and in 0·2M-acetate buffer (pH 5·0). Components were detected with aniline hydrogen phthalate,[8] alkaline silver nitrate,[10] and Chlorophenol Red.[11] These analyses indicated that fraction A contained oxalic and tartaric acid (trace), B contained tartaric and oxalic acid (trace), C contained glycollic and glyoxylic acid (trace), and D contained glyoxylic and glycollic acid.

A similar fractionation was carried out on a 0·1% solution of glycollic acid (4 l.) which had been irradiated for 12 hr. (total dose $2·3 \times 10^{19}$ ev ml.$^{-1}$). No compound other than glycollic, glyoxylic, tartaric, and oxalic acid was detected.

(iii) *Identification of major products.* Material A′ was dissolved in 2N-hydrochloric acid and reprecipitated at 100° in the presence of acetic acid by the addition of urea to the boiling solution. This process was repeated. Then the precipitate was suspended in excess of dilute sulphuric acid and extracted continuously with diethyl ether for 48 hr. The ethereal extract was evaporated and the residual oxalic acid recrystallised from a small volume of water (yield 60 mg.). It had m. p. 101°, raised to 188° (m. p. and mixed m. p.) after drying (P_2O_5; 60°/vac.; 3 hr.). It was heated with diphenylamine: the cooled melt, on extraction with ethanol, gave a blue solution which had an absorption spectrum ($\lambda_{max.}$ 604 mμ) identical with that of ethanolic Aniline Blue prepared from authentic oxalic acid in the same way.[12] 12·11 mg. of the acid neutralised 26·65 ml. of 0·01N-potassium hydroxide (phenolphthalein) (equiv., 45·5. Calc. for $H_2C_2O_4$: equiv., 45·0). The neutralised solution was concentrated until almost saturated, and to the hot solution was added hot ethanolic *S*-benzylthiuronium chloride (0·4 ml.; 1·5 g. of reagent in 10 ml. of ethanol). The solution was allowed to cool, and the crystalline product washed with a little water and ethanol. The bis-*S*-benzylthiuronium oxalate had m. p. and mixed m. p. 193° (Found: C, 51·1; H, 5·2; N, 13·5; S, 15·1. Calc. for $C_{18}H_{22}O_4N_4S_2$: C, 51·2; H, 5·3; N, 13·3; S, 15·2%).

A suspension of solid B′ (0·6 g.) in 2N-sulphuric acid (3·0 ml.) was stirred for 2 hr., freeze-dried, dried (P_2O_5) at 60° *in vacuo*, and boiled in ethanol. The ethanol solution was filtered and slowly evaporated, depositing crystals which on recrystallisation from ethanol and drying (P_2O_5) at 60° *in vacuo* gave tartaric acid (35 mg.), m. p. 202° [Found: equiv. (titration), 74·1. Calc. for $(HO{\cdot}CH{\cdot}CO_2H)_2$: 75·04]. The neutralised solution was concentrated until almost saturated, mixed with ethanolic *p*-nitrobenzyl bromide (0·1 g. in 1 ml.) and refluxed for 2 hr. Crystals which separated on cooling were recrystallised from aqueous ethanol (m. p. 146°) (Found: C, 51·5; H, 3·9; N, 6·8. Calc. for $C_{18}H_{16}O_{10}N_2$: C, 51·4; H, 3·8; N, 6·7%).

A solution of solid C′ (1·0 g.) was passed through a column of Zeo-Karb 225 (H^+ form) and freeze-dried. The residue was twice sublimed at 35° *in vacuo*, to yield glycollic acid (320 mg.), m. p. and mixed m. p. 79° (Found: equiv., 76·2. Calc. for $HO{\cdot}CH_2{\cdot}CO_2H$: equiv., 76·05). The *S*-benzylthiuronium salt had m. p. and mixed m. p. 145° (Found: C, 49·3; H, 5·6; N, 11·9; S, 13·2. Calc. for $C_{10}H_{14}O_3N_2S$: C, 49·6; H, 5·8; N, 11·6; S, 13·2%). The acid gave the characteristic violet colour [13] with 2 : 7-dihydroxynaphthalene in concentrated sulphuric acid at 100°.

Material D′ (0·2 g.) was treated as C′, giving the free acids which gave a strongly positive test with Schiff's reagent and the blue colour reaction [14] for glyoxylic acid with 2 : 3 : 4-trihydroxybenzoic acid in concentrated sulphuric acid at 50°. The acids (20 mg.) derived from D′ were dissolved in a solution of 2 : 4-dinitrophenylhydrazine (0·1 g.) in concentrated hydrochloric acid (18·2 ml.), diluted to 100 ml.; this gave glyoxylic acid 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 195° (Found: C, 38·0; H, 2·5; N, 22·1. Calc. for $C_8H_6O_6N_4$: C, 37·8; H, 2·4; N, 22·1%).

The small fractions E and F were not examined.

Irradiation of Glycollic Acid in the Presence of Oxygen.—(i) *Fractionation of the non-volatile products.* Glycollic acid (4 g.) in water (4 l.) was degassed as for the irradiation *in vacuo*. The solution was then saturated with oxygen for 2 hr., irradiated, with a continuous stream of

[10] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[11] Block, Durrum, and Zweig, "A Manual of Paper Chromatography and Paper Electrophoresis," Academic Press Inc., New York, 1955, p. 169.
[12] Feigl and Fehden, *Mikrochemie*, 1935, **18**, 272.
[13] Eegriwe, *Z. analyt. Chem.*, 1932, **89**, 123.
[14] *Idem, ibid.*, 1934, **100**, 325.

XUM

oxygen passing through it, for 24 hr. (total dose $5{\cdot}5 \times 10^{19}$ ev ml.$^{-1}$), freeze-dried, and fractionated as above, giving fractions A_O' (1·02 g.), B_O' (41 mg.), C_O' (3·4 g.), D_O' (0·75 g.), E_O' (35 mg.), and F_O' (10 mg.), the subscript o indicating irradiation in oxygen.

(ii) *Chromatography and ionophoresis.* These analyses gave similar results to those above, except that A_O contained no minor ingredients, and B_O was a much smaller fraction.

A similar analysis after 12 hours' irradiation showed glycollic, glyoxylic, and oxalic acid only.

(iii) *Identification of the major products.* Material A_O (oxalic acid) was prepared and identified as before, giving a positive test with diphenylamine,[12] equiv. 45·2, and m. p. and mixed m. p. 101° (189° anhydrous). The bis-*S*-benzylthiuronium salt had m. p. and mixed m. p. 194° (Found: C, 51·3; H, 5·1; N, 13·0. Calc. for $C_{18}H_{22}O_4N_4S_2$: C, 51·2; H, 5·3; N, 13·3%).

Material B_O was not present in sufficient quantity for characterisation.

Material C_O (glycollic acid), prepared as above, gave a positive test with 2 : 7-dihydroxynaphthalene,[13] equiv. 76·3, m. p. and mixed m. p. 78°, and a *S*-benzyl thiuronium salt, m. p. and mixed m. p. 145° (Found: C, 49·5; H, 5·8; N, 11·4. Calc. for $C_{10}H_{14}O_3N_2S$: C, 49·6; H, 5·8; N, 11·6%).

Material D_O (glyoxylic acid) gave positive reactions with Schiff's reagent and with 2 : 3 : 4-trihydroxybenzoic acid,[14] and a 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 195° (Found: C, 37·6; H, 2·5; N, 22·1. Calc. for $C_8H_6O_8N_4$: C, 37·8; H, 2·4; N, 22·1%).

Chromatography and Ionophoresis of the Non-volatile Products from Irradiated Solutions of Glyoxylic, Oxalic, and Tartaric Acids.—0·1% Solutions of glyoxylic acid, oxalic acid, and (+)-tartaric acid were irradiated in 20 ml. portions, each degassed as described above, (*a*) *in vacuo* or (*b*) in a stream of oxygen (dose-rate, $14{\cdot}2 \times 10^{16}$ ev min.$^{-1}$ ml.$^{-1}$ for 7 hr.; total, $5{\cdot}9 \times 10^{19}$ ev ml.$^{-1}$). After storage for 1 hr. the solutions were freeze-dried. Appreciable weight losses were observed with oxalic acid during irradiation both in a vacuum and in oxygen, and with glyoxylic acid during irradiation in the presence of oxygen.

The products were redissolved in water and subjected to paper chromatography and ionophoresis as described above.

In the presence of oxygen, glyoxylic acid gave only oxalic acid; in the absence of oxygen, a smaller amount of oxalic acid was formed, with slower-moving components having R_T 1·0 and 0·6. These last two components were detected by aniline hydrogen phthalate, Chlorophenol Red, and silver nitrate. Ionophoresis showed oxalic acid in both systems and a component with M_T 1 in the absence of oxygen.

Oxalic acid gave no products in the presence of oxygen, but, *in vacuo*, small amounts of a material having R_T 0·6 and M_T 1·0 were detected by all three reagents.

Tartaric acid in oxygenated solution showed colour development at R_T 1·0 with aniline hydrogen phthalate, and there were components behaving as mesoxalic and glyoxylic acid. In the absence of oxygen, colour development occurred at R_T 1·0 with aniline hydrogen phthalate and 0·3 with all three reagents. In addition, a component reacting with aniline hydrogen phthalate and silver nitrate, but not with Chlorophenol Red, was evident at R_T 1·5.

The authors thank the United Kingdom Atomic Energy Authority, Research Division, Harwell, for supporting these investigations and for maintenance grants, and Professor M. Stacey, F.R.S., and Dr. S. A. Barker for their interest.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, January 15th,* 1959.]

XUM

533. *Effects of γ-Radiation. Part III.* Quantitative Studies of the Products from Glycollic Acid.*

By P. M. Grant and R. B. Ward.

The decomposition of glycollic acid solutions induced by γ-radiation *in vacuo* and in the presence of oxygen has been followed quantitatively. The concentrations of glycollic, glyoxylic, tartaric, oxalic, and formic acid, formaldehyde, and carbon dioxide have been measured directly, and by new colorimetric methods in the cases of glycollic and glyoxylic acid. A mass balance for carbon has been obtained, and degradation pathways are advanced to explain the results.

It has been shown * that the main non-volatile degradation products formed on γ-irradiation of glycollic acid in dilute aqueous solution in the presence and in absence of oxygen are glyoxylic, tartaric, and oxalic acid, the effect of oxygen being to reduce greatly the yield of tartaric acid.

In this work an attempt has been made to determine the above-mentioned products, together with the volatile products, directly and *in situ* by methods which, within the system studied, are specific for each product. This has involved developing methods for colorimetric determination of glycollic and glyoxylic acid, and finding suitable conditions for the estimation of tartaric and oxalic acid by adaptations of previous methods. The colorimetric methods adopted for glycollic and glyoxylic acids are based on two " spot " tests developed by Eegriwe, using 2 : 7-dihydroxynaphthalene and 2 : 3 : 4-trihydroxybenzoic acid respectively.[1,2,3]

2 : 7-Dihydroxynaphthalene in concentrated sulphuric acid solution, gives with glycollic acid a violet colour when heated for 30 min. in a stoppered tube at 100°. The calibration curve was not quite linear (Table 3), necessitating the use of the curve to convert Spekker readings into glycollic acid content. Standard determinations were included since the colour varied a little (reading ±0·01) for different preparations of the reagent. Measurement of known mixtures of the radiation products showed that both glyoxylic and oxalic acid slightly increased the optical density, while tartaric acid decreased it. The effect of oxalic acid is negligible; the effects of glyoxylic and tartaric acid may be ignored when their respective proportions do not exceed 20% and 50% of the glycollic acid in the sample. When present in equal amounts (Table 3) the estimated error was +11·2% and −4·1% respectively.

2 : 3 : 4-Trihydroxybenzoic acid and glyoxylic acid in the presence of sulphuric acid at 50° (30 min.) gave a blue colour. The calibration curve was linear (Table 4), but standard determinations were included. Very considerable variation in colour was found with various samples of sulphuric acid (Table 4), indicating that some contaminant, *e.g.*, iron or selenium, present in traces was essential for development of the colour. The reagent, furthermore, tended to be unstable in sulphuric acid. Best results were obtained when finely powdered solid reagent was added to the aliquot part of glyoxylic acid solution in a test-tube, followed by a measured volume of sulphuric acid. The test-tube was then stoppered, shaken, and immersed in a water-bath at 50°. In mixtures of known composition the presence of an equal quantity of oxalic acid had no detectable effect. Tartaric acid decreased the colour formed to a small extent, the effect at equal concentrations was to introduce an error in the glyoxylic acid determination of −2·6% (Table 4). Glycollic

* Part II, preceding paper.

[1] Eegriwe, *Z. analyt. Chem.*, 1932, **89**, 123.
[2] *Idem*, *ibid.*, 1934, **100**, 325.
[3] Feigl, " Spot Tests," Vol. II, Organic Applications, 4th English Edn., Elsevier Publ. Co., Amsterdam, 1954, pp. 249, 253.

XUM

TABLES 1 & 2. *Irradiation of glycollic acid solutions.*

Time (hr.)	Total dose (10^{18} ev ml.$^{-1}$)	Glycollic acid destroyed mmole/l.	Glycollic acid destroyed (%)	Radiation product yields: Glyoxylic acid hydrate (mmole/l.)	Oxalic acid dihydrate (mmole/l.) (corr.)	Tartaric acid (corr.) (mmole/l.)	Tartaric acid Mol. conv.†	Formaldehyde (mmole/l.)	Formaldehyde Mol. conv.†	Formic acid (mmole/l.)	Formic acid Mol. conv.†	Carbon dioxide (mmole/l.)	Carbon dioxide Mol. conv.†	Carbon balance data: Total glycollic acid accounted for (mmole/l.)	Carbon balance data: Discrepancy (%)
						TABLE 1. *Irradiation in a vacuum.*									
0·25	0·57	0·066	0·5	0·0217	—	0·018	0·036	0·01	0·005	—	—	—	—	—	—
0·5	1·15	0·132	1·0	0·0353	—	0·039	0·078	0·01	0·005	0·01 *	0·005 *	0·01 *	0·005 *	0·128	−3
0·75	1·7	0·172	1·3	0·0484	—	0·065	0·130	0·012	0·006	—	—	—	—	—	—
1·0	2·3	0·238	1·8	0·0641	—	0·079	0·158	0·014	0·007	0·02 *	0·01 *	0·021	0·0105	0·250	+5
1·5	3·4	0·369	2·8	0·0945	—	0·117	0·234	—	—	—	—	—	—	—	—
2·0	4·6	0·475	3·6	0·1185	—	0·145	0·290	0·015	0·008	0·03 *	0·015 *	0·0345	0·0173	0·449	−5
2·5	5·7	0·607	4·6	0·128	—	0·192	0·383	—	—	—	—	—	—	—	—
3·0	6·9	0·74	5·6	0·145	—	0·237	0·473	—	—	—	—	0·0543	0·0272	—	—
4·0	9·2	0·96	7·3	0·165	—	0·337	0·673	0·014 *	0·007 *	0·05 *	0·025 *	0·0613	0·0307	0·901	−6
5·0	11·5	1·20	9·1	0·201	0·0092	0·425	0·850	—	—	—	—	0·0843	0·0422	—	—
8·0	18·5	1·73	13·1	0·251	0·0382	0·66	1·31	0·013	0·007	0·09 *	0·045 *	0·138	0·069	1·72	−1
10·0	23	2·05	15·5	0·278	0·0530	0·88	1·76	—	—	—	—	—	—	—	—
12·0	27·5	2·31	17·5	0·283	0·0728	0·97	1·93	0·013 *	0·007 *	0·15	0·075	0·205	0·1025	2·47	+7
18·0	41	3·14	23·8	0·278	0·145	1·37	2·74	—	—	—	—	0·295	0·148	—	—
24·0	55	3·88	29·4	0·272	0·259	1·72	3·43	0·013	0·007	0·28	0·14	0·363	0·182	4·29	+11
						TABLE 2. *Irradiation in oxygen.*									
0·25	0·57	—	—	0·0263	—	—	—	0·009	0·005	—	—	0·0198	0·0099	—	—
0·5	1·150	0·092	0·7	0·0540	—	—	—	0·011	0·006	0·04 ‡	0·02 ‡	0·032	0·016	0·096	+4
0·75	1·70	—	—	0·0842	—	—	—	0·012	0·006	—	—	0·055	0·0275	—	—
1·0	2·3	0·172	1·3	0·106	—	—	—	0·018	0·009	0·063	0·032	0·072	0·036	0·183	+6
1·5	3·4	0·264	2·0	0·156	—	—	—	—	—	—	—	0·117	0·0585	—	—
2·0	4·6	0·36	2·7	0·202	—	—	—	0·017	0·009	0·15	0·075	0·153	0·0765	0·363	+1
2·5	5·7	0·435	3·3	0·238	—	—	—	—	—	—	—	0·188	0·094	—	—
3·0	6·9	0·53	4·0	0·276	—	—	—	—	—	—	—	0·216	0·108	—	—
4·0	9·2	0·69	5·2	0·324	—	0·0061	0·0122	0·018 ‡	0·009 ‡	0·30	0·15	0·316	0·158	0·653	−5
5·0	11·5	0·83	6·3	0·388	—	0·0082	0·0164	—	—	—	—	0·378	0·189	—	—
8·0	18·5	1·23	9·3	0·552	0·0138	0·0132	0·0264	0·019	0·01	0·53	0·27	0·633	0·317	1·189	−3
12·0	27·5	1·77	13·4	0·711	0·0461	0·0198	0·0396	0·018 ‡	0·009 ‡	0·95	0·48	1·06	0·53	1·816	+3
18·0	41	2·47	18·7	0·870	0·135	0·0343	0·0686	—	—	—	—	1·71	0·86	—	—
24·0	55	3·10	23·5	0·962	0·286	0·0383	0·0766	0·017	0·009	1·68	0·84	2·50	1·25	3·42	+10

* Determined from Fig. 1. ‡ Determined from Fig. 2. † Molar conversion: mmole of glycollic acid required to produce observed yield of the particular component on the basis of complete conversion solely into this component.

acid, however, when present to the extent of 1000 parts of glycollic acid to one part of glyoxylic acid, introduced an error in the glyoxylic acid estimation of only +1·4%.

Tartaric acid was determined by means of its uptake of periodate.[4] At room temperature over-oxidation occurred, which was reduced by oxidation at 5° and still further by addition of glycollic acid. There was no interference by oxalic acid; glyoxylic acid showed a tendency to increase the periodate uptake, even at 5°. Addition of glycollic acid (100 times the amount of tartaric acid present) reduced the oxidation of glyoxylic acid at 5° to a negligible value (Table 5), probably because it increased acidity.

Oxalic acid was determined by precipitation of the calcium salt. To prevent co-precipitation of calcium tartrate, the tartaric acid (previously estimated as above) was destroyed by treating the sample for oxalic estimation with a 10% molar excess of sodium metaperiodate before precipitating the calcium oxalate with calcium chloride. The calcium oxalate was washed and estimated titrimetrically with potassium permanganate. Analysis of known mixtures under standard conditions showed that the values obtained

FIG. 1.

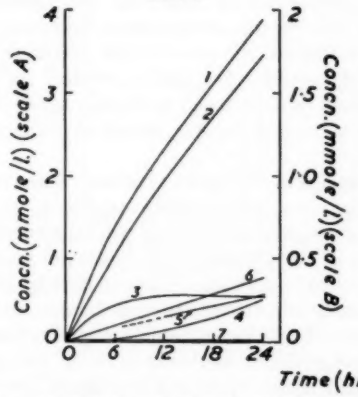


FIG. 2.

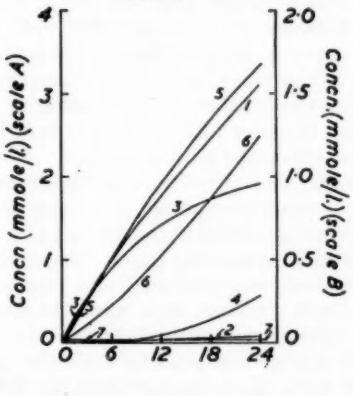


FIG. 1. *γ-Irradiation of glycollic acid solutions* in vacuo. (*Dose rate*, 2·3 × 10^{18} ev $ml.^{-1}$ $hr.^{-1}$).
Scale A: 1, *Glycollic acid destroyed. Scale B*: 2, *Tartaric acid*; 3, *glyoxylic acid*; 4, *oxalic acid*; 5, *formic acid*; 6, CO_2; 7, CH_2O.

FIG. 2. *γ-Irradiation of glycollic acid solutions in oxygen.* (*Dose rate as for Fig.* 1.)
Scale A: *curves* 1 *and* 6. *Scale B*: *curves* 2—5 *and* 7. *Numerals as for Fig.* 1.

were consistently about 5 mg. below the true value. This correction for solubility and manipulation was therefore used in each determination.

Early analyses of irradiated solutions showed that more glycollic acid was being destroyed than was accounted for by the glyoxylic, tartaric, and oxalic acid formed, indicating additional volatile products. Attention was turned to formaldehyde, volatile acids (determined as formic acid), and carbon dioxide. Formaldehyde was determined by means of chromotropic acid.[5] Only glyoxylic acid interfered and this was not serious while the glyoxylic acid content of the irradiated solution remained small.

Volatile acid was determined by estimating the acidity in the frozen sublimate obtained on freeze-drying of the irradiated solution. Appreciable quantities of glycollic acid collected in the sublimate, so this was measured by the 2:7-dihydroxynaphthalene method, and its acidity component subtracted from the total acidity of the sublimate: the difference was expressed as formic acid.

Carbon dioxide was determined by passing a stream of nitrogen through the boiling

[4] Dyer, "Methods of Biochemical Analysis, Vol. III," Interscience Publ., Inc., New York, 1956 p. 111.
[5] MacFadyen, *J. Biol. Chem.*, 1945, **158**, 107.

XUM

solution. The gas stream then passed through a reflux condenser into a two-stage sintered-glass trap containing barium hydroxide. The carbon dioxide was estimated by back-titration of the barium hydroxide solution to phenolphthalein.

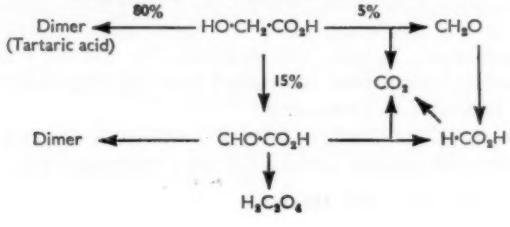
The results of these analyses are summarised in Tables 1 (evacuated system) and 2 (oxygenated system). Concentrations of the products are shown in Figs. 1 and 2. The carbon balance was obtained by adding together the amounts of glycollic acid required to yield the observed products and expressing this as a percentage excess (positive) or deficiency (negative) compared with the observed destruction of glycollic acid. In some cases certain quantities have been obtained, where indicated, by measurement from Figs. 1 and 2.

The small discrepancies in the carbon balance are considered to indicate an effectively complete analysis. As the degradation proceeds, at least three factors tending to produce high results become apparent. Increasing yields of tartaric acid and further radical addition to produce trimer molecules will each cause high values for tartaric acid. Also, all calculations for the non-volatile products were based on the assumption that there is no change in weight of the non-volatile solute, since the increase in weight associated with the formation of glyoxylic acid and oxalic acid approximately balanced the formation of volatile components. However, the yield of the volatile components becomes proportionally larger as the reaction proceeds, so estimates of non-volatile products exceed the true value, particularly in the oxygenated system. Detailed numerical analysis of the systems showed that no significant error would be introduced until after approximately 12 hr., and the error introduced then is of the same order as the observed discrepancy in the carbon balance in both systems.

It is concluded, therefore, that the discrepancies in the carbon balance, while at times larger than would be expected from experimental error, can be explained logically.

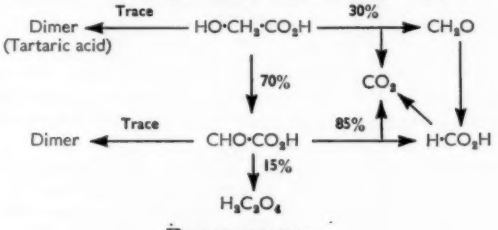
The results obtained in the absence of oxygen agreed completely with the mechanisms advanced in the preceding paper. Some 80% of the glycollic acid destroyed reappeared as tartaric acid, which behaved as a relatively stable product. Approximately 15% was converted into glyoxylic acid, while the remaining 5% formed carbon dioxide and either formaldehyde or formic acid. Since the content of formaldehyde rapidly reached a stationary low level within 1 hr. while the formic acid increased continuously, the acid was produced from the relatively unstable formaldehyde. The tartaric acid appeared to undergo little change, its rate of formation closely following the decreasing glycollic acid concentration. Glyoxylic acid was less stable and reached a stationary level after 9 hr. Oxalic acid appeared as a typical secondary product (Fig. 1) and glyoxylic acid had been shown (preceding paper) to give oxalic acid on irradiation *in vacuo*, as well as products of higher molecular weight. The rates of formation of formic acid and carbon dioxide were too great to be accounted for merely by the yield directly from glycollic acid, and also the yields increased with time, suggesting their formation to be partly primary and partly secondary. These observations indicated that some of the glyoxylic acid was degraded to carbon dioxide and formic acid. Since the mechanisms suggested should yield formic acid and carbon dioxide in almost equimolecular quantities, the progressively increasing divergence in Fig. 1 indicates that degradation of formic acid gives carbon dioxide, as illustrated in Scheme A.

SCHEME A. *Degradation* in vacuo.



The degradation in oxygen had a similar course except (cf. preceding paper) that there was very little formation of C–C linkages (including polymerisation [6]) since peroxy-radicals are formed.[7] This made it possible to estimate the relative extent of degradation of glyoxylic acid by the two pathways. The degradation may be expressed as in Scheme B. It will be seen that relatively a greater proportion of C–C linkages are broken. Higher levels of glyoxylic acid and formaldehyde are established, as would be expected from the greater proportions produced. Since a very much higher proportion of relatively labile products is formed than in the evacuated system (where tartaric acid accounted for 80%), a larger proportion of the solvent-radical yield is consumed in effecting secondary and tertiary degradations, as may be seen from the higher yields of carbon dioxide and formic acid. This results in a lower overall rate of degradation of glycollic acid, although the total amount of oxidation is larger in the oxygenated system.

SCHEME B. *Degradation in presence of oxygen.*



EXPERIMENTAL

Analytical Methods.—(i) *Determination of glycollic acid.* 0—100 μl. of glycollic acid solution (0·5 mg./ml.) were placed in a test-tube by using an Agla Micrometer Syringe and made up (if necessary) to 100 μl. with water (100—0 μl.). 10 ml. of a freshly prepared solution of 2 : 7-dihydroxynaphthalene [1] in concentrated sulphuric acid (10 mg./100 ml.) were added, the tubes were stoppered, swirled, and then heated in a boiling-water bath for 30 min. The tubes were cooled and the violet colour measured in 1 cm. cells, in a Hilger " Spekker " spectrophotometer, with a yellow-green filter (No. 605; 550 mμ). A solution with glycollic acid solution omitted [but containing water (100 μl.)] was used as the control (Table 3).

TABLE 3. *Calibration of glycollic acid: interference tests.*

Glycollic acid alone (μg.)	" Spekker " reading	Glycollic acid (μg.)	Glyoxylic acid hydrate (μg.)	Oxalic acid dihydrate (μg.)	Tartaric acid (μg.)	" Spekker " reading
2·5	0·058	25·0	—	—	—	0·605
5·0	0·131	25·0	5·0	—	—	0·619
12·5	0·329	25·0	12·5	—	—	0·634
25·0	0·605	25·0	25·0	—	—	0·673
37·5	0·797	25·0	—	12·5	—	0·606
50·0	1·001	25·0	—	25·0	—	0·609
		25·0	—	—	12·5	0·596
		25·0	—	—	25·0	0·580
		25·0	2·5	2·5	2·5	0·608
		25·0	8·3	8·3	8·3	0·613
		12·5	—	—	—	0·329
		12·5	12·5	12·5	12·5	0·374

The interference of glyoxylic, oxalic, and tartaric acid was ascertained by adding suitable volumes (0—50 μl.) of aqueous solutions of these acids (0·5 mg./ml.) to 25 or 50 μl. of 0·05% glycollic acid solution. The volumes were made up to 100 μl. and the glycollic acid determined (Table 3). Standard determinations were necessary with each batch of estimations, the variation between batches being $< \pm 0{\cdot}01$.

(ii) *Determination of glyoxylic acid.* 0—100 μl. of glyoxylic acid hydrate solution (0·5

[6] Barker, Grant, Stacey, and Ward, *J.*, 1959, 2648.
[7] Johnson, Scholes, and Weiss, *J.*, 1953, 3091; Dewhurst, Samuel, and Magee, *Radiation Res.*, 1954, **1**, 62; Garrison, Haymond, and Weeks, *ibid.*, p. 97.

XUM

mg./ml.) was placed in a test-tube by means of a micrometer syringe and made up to 100 µl. with water. Finely powdered 2 : 3 : 4-trihydroxybenzoic acid [2] (25·0 mg.) was added, followed by concentrated sulphuric acid (10 ml.). The mixture was shaken for about 15 sec. and immersed, stoppered, into a water-bath at 50°. After 30 min. the tube was cooled, and the blue colour measured in 1 cm. cells, in a " Spekker " spectrophotometer with yellow filters (No. 606; 575 mµ). A solution with glyoxylic acid solution omitted [but containing water (100 µl.)] was used as control (Table 4).

TABLE 4. *Calibration of glyoxylic acid: interference tests.*

Glyoxylic acid hydrate alone (µg.)	" Spekker " reading	Glyoxylic acid hydrate (µg.)	Glycollic acid (µg.)	Oxalic acid dihydrate (µg.)	Tartaric acid (µg.)	" Spekker " reading
2·5	0·072	25·0	—	—	—	0·588
5·0	0·124	25·0	1,700	—	—	0·586
12·5	0·302	25·0	4,400	—	—	0·594
25·0	0·588	25·0	20,000	—	—	0·596
37·5	0·850	25·0	—	5·0	—	0·582
50·0	1·047	25·0	—	25·0	—	0·585
		25·0	—	—	5·0	0·586
		25·0	—	—	12·5	0·576
		25·0	—	—	25·0	0·573
		12·5	—	—	—	0·302
		12·5	5,000	18·75	18·75	0·308
		25·0	Various samples of sulphuric acid supplied by Messrs. Peyton and Son			0·570—0·621
		25·0	B.D.H. " AnalaR " sulphuric acid			0·238
		25·0	B.D.H. " MAR " sulphuric acid			0·029

The interference of glycollic, oxalic, and tartaric acid was ascertained by adding dry glycollic acid (0—20 mg.) and suitable volumes of aqueous solutions of oxalic acid dihydrate and tartaric acid (0·5 mg./ml.) to 25 or 50 µl. of 0·05% glyoxylic acid hydrate solution. The volumes were made up to 100 µl. and the glyoxylic acid determined. Standard determinations were necessary with each batch of estimations. The colour produced was reduced very markedly when samples of sulphuric acid purer than available commercial grades were used. The reduction in colour with " AnalaR " and " MAR " reagent grades is shown in Table 4.

(iii) *Determination of tartaric acid.* The samples were dissolved in water (*ca.* 30 ml.). 0·1M-Sodium metaperiodate (10 ml.) was added and the solution made up to 50 ml. with water. The solutions were kept throughout at 5°. Aliquot parts (5 ml.) were removed at intervals, and sodium hydrogen carbonate (0·5 g.), an excess of 0·02N-sodium arsenite (20 ml.) and 20% aqueous potassium iodide (1 ml.) were added. The excess of arsenite was titrated after 10 min. with 0·021N-iodine (sodium–starch glycollate). A control determination was made without the tartaric acid. The periodate consumption was then determined from the difference titre. The results for some known mixtures are shown in Table 5, which also shows the improvement due to lowering the reaction temperature to 5°. Analytical results were determined after 5 min., and the value divided by 1·03 to correct for the slight over-oxidation.

TABLE 5. *Calibration of tartaric acid: interference tests.*

Temp.	Tartaric acid (mg.)	Glycollic acid (mg.)	Glyoxylic acid hydrate (mg.)	Oxalic acid dihydrate (mg.)	Periodate uptake (mmole per mmole of tartaric acid) at: 5 min.	15 min.	30 min.	60 min.
15°	20·0	—	—	—	1·36	1·83	2·18	2·48
15	50·0	—	—	—	1·15	1·40	1·68	1·80
15	—	5000	—	—	0·0011 *	0·0014 *	0·0017 *	0·002 *
15	—	—	50·0	—	0·2 *	0·35 *	0·5 *	0·64 *
15	—	—	—	50·0	Nil	Nil	Nil	Nil
15	50·0	5000	—	—	1·02	1·08	1·18	1·30
15	50·0	5000	50·0	50·0	1·13	1·25	1·32	1·57
5	50·0	5000	50·0	50·0	1·03	1·06	1·09	1·13
5	25·0	5000	25·0	10·0	1·02	1·05	1·09	1·11
5	25·0	500	10·0	10·0	1·05	1·08	1·12	1·16

* Expressed as uptake in mmole per mmole of solute.

XUM

(iv) *Determination of oxalic acid.* This was effected after the tartaric acid content had been ascertained. The sample was dissolved in water, and 0·1N-sodium metaperiodate added until 1·1 mmole of the oxidant were present for each mmole of tartaric acid. The solution was heated to 60°, and 5% calcium chloride hexahydrate solution (50 ml.) added. The solution was neutralised with aqueous ammonia and kept for 10 min., and glacial acetic acid (5 ml.) was added. The solution was stirred for 10 min., then filtered through a No. 4 sintered-glass crucible, and the precipitate was washed with water, 4N-acetic acid, and again water, and was extracted with 2N-sulphuric acid (10 × 10 ml.); the extract was titrated with 0·0954N-potassium permanganate at 60°.

Four solutions, each containing glycollic acid (4 g.), glyoxylic acid hydrate (50 mg.), tartaric acid (50 mg.) and oxalic acid dihydrate (severally 100, 50, 25, and 10 mg.) were estimated to contain 94·0, 47·5, 20·6, and 4·4 mg. of oxalic acid dihydrate respectively. Under carefully controlled conditions a loss of *ca.* 5 mg. was obtained in each determination irrespective of the oxalic acid content. Corrected estimations for the above solutions would therefore be 99 (99%), 52·5 (105%), 25·6 (102%), and 9·4 (94%), respectively.

(v) *Determination of formaldehyde.* Aliquot parts (1 ml.) of solution were heated at 100° for 30 min. with chromotropic acid reagent.[5] The colour was determined with a "Spekker" spectrophotometer (yellow filter, No. 606). The formaldehyde was then found from a calibration curve determined from known amounts of formaldehyde. Suitable control determinations showed glyoxylic acid to interfere, but only when its concentration was excessive: correction was made.

(vi) *Determination of formic acid.* A suitable volume of the irradiated solution was freeze-dried and the sublimate titrated with standard alkali. Glycollic acid in the sublimate was determined as described above, and the difference in these two determinations was expressed as formic acid. The other acids (glyoxylic, tartaric, and oxalic) present in the irradiated solutions were absent from the sublimate.

(vii) *Determination of carbon dioxide.* Nitrogen was passed into the irradiation vessel containing the solution which had been irradiated *in vacuo*. The gas, after passing through the solution and a reflux condenser, was bubbled through a two-stage sintered-glass absorption vessel containing N-barium hydroxide. The solution was boiled for an hour to expel carbon dioxide, which was estimated by back-titration of the alkali with 1·02N-hydrochloric acid (phenolphthalein). When oxygen was passed through the solution during irradiation, the waste gas-stream was passed through the absorption vessel containing barium hydroxide throughout the irradiation.

Preparation of Irradiated Samples.—0·1% Glycollic acid solution (4 l.) was prepared for irradiation and irradiated *in vacuo* and in the presence of oxygen as described in the preceding paper. A sample (*ca.* 5 ml.) was removed for determination of glycollic acid and formaldehyde, and the remainder freeze-dried for determination of glyoxylic, tartaric, and oxalic acid. A further batch was freeze-dried for determination of formic acid, and another 4 l. of irradiated solution was used to measure the carbon dioxide.

Analytical Results.—The analyses are summarised in Tables 1 and 2. The *G* values for the various products are given in Table 6.

TABLE 6. *G Values.*

Product	Vac.	In O_2	Product	Vac.	In O_2
Glycollic acid	−6·1	−4·5	Carbon dioxide	0·5	1·9
Glyoxylic acid	1·5	2·75	Formic acid	0·5	1·6
Tartaric acid	2·1	0·04			

The authors thank the United Kingdom Atomic Energy Authority, Research Division, Harwell, for supporting these investigations and for maintenance grants, and Professor M. Stacey, F.R.S., and Dr. S. A. Barker for their interest.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, January 15th*, 1959.]

XUM

534. *Molecular Polarisability. The Molar Kerr Constants of Certain Derivatives of Diphenyl.*

By J. Y. H. Chau, (Mrs.) C. G. Le Fèvre, and R. J. W. Le Fèvre.

The molar Kerr constants of diphenyl and its 4-fluoro-, -chloro-, -bromo-, -iodo-, -nitro-, and 2 : 2′- and 3 : 3′-dinitro-derivatives are reported and discussed. They indicate a rough orthogonality of configuration for the last two molecules, and may be reconciled with flat configurations for the first six, among which conjugation is presumably causing a polarisability exaltation parallel to the 1 : 1′-bond.

The measurements now recorded were started in the hope that they would assist decisions on the configurations adopted by diphenyl and certain of its derivatives when present as solutes at room temperatures.

The last thirty years' literature shows that configuration in this series is strongly affected by substitution. The diphenyl skeleton was originally expected by Le Fèvre and Turner [1] to possess a tendency to planarity owing to conjugation, opposed by the volumes and electrical effects of substituents; the hydrocarbon itself is now known by *X*-ray analysis and electron diffraction to be planar [2] in the crystal but non-planar [3] in the vapour. Dipole moments [4] in solution have indicated that 2 : 2′-dinitrodiphenyls have their rings rotated out of the *cis*-position so that the angles between them range from 70° to 90° and that these (azimuthal) angles are exceeded in the corresponding 3 : 3′-isomers. In gaseous 2 : 2′-dihalogeno-diphenyls [5] the azimuthal angles are about 75°, as in crystalline [6] 2 : 2′-dichlorobenzidine (72°) and [7] *m*-tolidine dihydrochloride (71°); yet while 3 : 3′-dichlorobenzidine is [3] non-planar (*ca.* 52°) as a gas, it is stated [8] as a solid to have the chlorine atoms disposed *trans* in a model which is flat or nearly so. No information by the above methods appears to exist concerning the configurations of 4-monosubstituted diphenyls.

Present Measurements.—Standard techniques being used,[9,10] the dielectric constants, densities, electric double refractions, etc., have been observed for solutions of the solutes named in Tables 1 and 2. Symbols are defined in refs. 9 and 10.

The dipole moments of the five monosubstituted diphenyls in Table 2 have the slight novelty of being determined in carbon tetrachloride instead of benzene.[4,11] The values are qualitatively consistent with past studies of relationships between polarisation and medium (cf. ref. 9, Chap. III).

Discussion.—It is of interest to compare experimental molar Kerr constants with those calculable from known bond or group polarisabilities. Data by Le Fèvre and Purnachandra Rao [12] are relevant. For example, in computing ${}_mK$ for 2 : 2′- or 3 : 3′-dinitrodiphenyl, use can be made of the molecular semi-axes reported for nitrobenzene,[12] *viz.*, $b_1 = 1{\cdot}617$, $b_2 = 1{\cdot}200$, and $b_3 = 0{\cdot}862 \times 10^{-23}$ c.c., where b_1 lies collinear with $\mu_{\text{resultant}}$, b_2 collinear with the 2 : 6 direction, and b_3 perpendicular to the molecular plane.

[1] Le Fèvre and Turner, *Chem. and Ind.*, 1926, **45**, 831.
[2] Dhar, *Proc. Nat. Inst. Sci. India*, 1949, **15**, 11.
[3] Bastiansen, *Acta Chem. Scand.*, 1949, **3**, 408.
[4] Le Fèvre and Le Fèvre, *J.*, 1936, 1130; Le Fèvre and Vine, *J.*, 1938, 967; Weissberger, Sängewald, and Hampson, *Trans. Faraday Soc.*, 1934, **30**, 884; Littlejohn and Smith, *J.*, 1953, 2456, 1954, 2552.
[5] Bastiensen, *Acta Chem. Scand.*, 1950, **4**, 926.
[6] Smare, *Acta Cryst.*, 1948, **1**, 150.
[7] Fowweather and Hargreaves, *ibid.*, p. 81.
[8] Toussaint, *ibid.*, p. 43.
[9] Le Fèvre, "Dipole Moments," Methuen, London, 3rd Edn., 1953.
[10] Le Fèvre and Le Fèvre, *Rev. Pure Appl. Chem.*, 1955, **5**, 261.
[11] Wesson, "Tables of Electric Dipole Moments," Technology Press, Massachusetts Institute of Technology, 1948.
[12] Le Fèvre and Purnachandra Rao, *J.*, 1958, 1465.

XUM

TABLE 1. *Dielectric polarisations, Kerr effects, etc., at 25°.*

*Diphenyl in carbon tetrachloride.**

10^5w_2	778	969	1762	2712	3464	4196
ε_{12}	2·2315	2·2326	—	—	2·2470	2·2518
d_{12}	1·5784	1·5771	—	—	1·5568	1·5505
n_{12}	1·4594	1·4601	—	—	1·4658	1·4679
$10^7\Delta B$	0·018	0·023	0·041	0·064	$0·080_5$	0·097

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 0·585$, $\Sigma\Delta d/\Sigma w_2 = -0·799_4$, $\Sigma\Delta n/\Sigma w_2 = 0·246_6$, $10^7\Delta B = 2·37_9w_2 - 1·41w_2^2$.

*4-Fluorodiphenyl in carbon tetrachloride.**

10^5w_2	227	266	295	304	329	411
ε_{12}	2·2335	2·2345	2·2353	2·2363	2·2366	2·2384
d_{12}	1·5830	—	1·5825	1·5825	1·5823	—
10^5w_2	480	818	885			
n_{12}	1·4584	1·4589	1·4596			
10^5w_2	176	245	724	795	901	1465
$10^7\Delta B$	0·023	0·033	0·096	0·103	0·118	0·192

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 2·87_1$, $\Sigma\Delta d/\Sigma w_2 = -0·666_7$, $\Sigma\Delta n/\Sigma w_2 = 0·183_2$, $\Sigma\Delta B/\Sigma w_2 = 13·1_3$.

*4-Chlorodiphenyl in carbon tetrachloride.**

10^5w_2	384	412	561	725	734	1223	1232	1534
ε_{12}	2·2399	2·2403	2·2445	2·2506	2·2518	2·2671	2·2665	2·2778
d_{12}	1·5820	1·5818	1·5809	1·5806	1·5797	1·5773	1·5770	1·5700
10^5w_2	394	395	650					
n_{12}	1·4582	1·4583	1·4589					
10^5w_2	209	366	637	846	902	997		
$10^7\Delta B$	0·043	0·082	0·126	0·185	0·187	0·214		

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 3·27_0$, $\Sigma\Delta d/\Sigma w_2 = -0·686_2$, $\Sigma\Delta n/\Sigma w_2 = 0·201_8$, $\Sigma\Delta B/\Sigma w_2 = 21·1_8$.

*4-Bromodiphenyl in carbon tetrachloride.**

10_5w_2	375	392	554	767	813	1058	1249	1598
ε_{12}	2·2380	2·2385	2·2433	2·2500	2·2514	2·2576	2·2630	2·2710
d_{12}	1·5834	1·5832	1·5831	1·5826	1·5825	1·5820	1·5815	1·5807
10^5w_2	308	324	365					
n_{12}	1·4583	1·4584	1·4585					
10^5w_2	54	156	402	445	569	614		
$10^7\Delta B$	0·008	0·027	0·073	0·080	0·107	0·115		

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 2·89_1$, $\Sigma\Delta d/\Sigma w_2 = -0·249_3$, $\Sigma\Delta n/\Sigma w_2 = 0·270_8$, $\Sigma\Delta B/\Sigma w_2 = 18·3_0$.

*4-Iododiphenyl in carbon tetrachloride.**

10^5w_2	46	49	86	88	102	104
ε_{12}	2·2280	2·2280	2·2286	2·2287	2·2291	2·2291
d_{12}	1·5845	1·5845	1·5845	1·5844	1·5844	1·5844
n_{12}	1·4576	1·4576	—	—	—	1·4578
$10^7\Delta B$	0·010	0·011	0·020	0·020	0·021	0·021

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 2·00$, $\Sigma\Delta d/\Sigma w_2 = -0·063$, $\Sigma\Delta n/\Sigma w_2 = 0·301_3$, $\Sigma\Delta B/\Sigma w_2 = 21·7$.

*4-Nitrodiphenyl in carbon tetrachloride.**

10^5w_2	39	56	94	132	175	211
$10^7\Delta B$	0·062	0·084	0·144	0·205	0·266	0·326
10^5w_2	185	230	385			
n_{12}	1·4579	1·4580	1·4586			

whence $\Sigma\Delta B/\Sigma w_2 = 153·7$, $\Sigma\Delta n/\Sigma w_2 = 0·250_9$.

2 : 2′-Dinitrodiphenyl in benzene.†

10^5w_2	418	829	1112	1297	1301
$10^7\Delta B$	−0·083	−0·158	−0·205	−0·252	−0·255

whence $\Sigma\Delta B/\Sigma w_2 = -19·22$.

3 : 3′-Dinitrodiphenyl in benzene.†

10^5w_2	171	172	174	212	214	268
ε_{12}	2·2856	2·2859	2·2859	2·2885	2·2889	2·2938
d_{12}	0·8744	0·8744	0·8744	0·8745	0·8746	0·8748
10^5w_2	249	268	373	398		
n_{12}	1·4978	1·4978	1·4979	1·4980		
10^5w_2	33	50	65	76	80	82
$10^7\Delta B$	−0·005	−0·009	−0·012	−0·014	−0·014	−0·015

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 7·72_9$, $\Sigma\Delta d/\Sigma w_2 = 0·355_0$, $\Sigma\Delta n/\Sigma w_2 = 0·085_4$, $\Sigma\Delta B/\Sigma w_2 = -17·8_4$.

* For $w_2 = 0$, $\varepsilon^{25} = 2·2270$, $d_4^{25} = 1·5845$, $n_D^{25} = 1·4575$, $B_D^{25} = 0·070 \times 10^{-7}$.

† For $w_2 = 0$, $\varepsilon^{25} = 2·2725$, $d_4^{25} = 0·8738$, $n_D^{25} = 1·4976$, $B_D^{25} = 0·410 \times 10^{-7}$.

XUM

TABLE 2. *Calculation of results.*

Solute	$\alpha\varepsilon_1$	β	γ	δ	$_{\infty}P_2$ (c.c.)	$_{D}P$ (c.c.)	μ (D)	$10^{-12}{}_{\infty}({}_{m}K_2)$
Diphenyl	0·585	$-0{\cdot}504_5$	0·169	$33{\cdot}9_9$	$52{\cdot}0_6$	(52·1)	*ca.* 0	40·5
4-Fluoro-	$2{\cdot}87_1$	$-0{\cdot}420_8$	0·126	187·4	$97{\cdot}2_9$	51·8 [a]	$1{\cdot}4_9$	242
4-Chloro- ,, ...	$3{\cdot}27_9$	$-0{\cdot}433_1$	0·138	302·1	114·8	57·0 [a]	$1{\cdot}6_5$	426
4-Bromo- ,, ...	$2{\cdot}89_1$	$-0{\cdot}157_7$	0·186	261·4	120·8	60·0 [a]	$1{\cdot}7_2$	456
4-Iodo- ,, ...	2·00	$-0{\cdot}063$	0·207	310	112·7	65·6 [a]	$1{\cdot}5_3$	671
4-Nitro- ,, ...	18·92 [b]	$-0{\cdot}477_5$ [b]	0·172	2196	453·3	57·9 [a]	$4{\cdot}4_9$	3265
2 : 2′-Dinitro- [c]	12·43	$0{\cdot}367_9$ [d]	0·057 [d]	$-46{\cdot}8_5$	623·6	63·8 [a]	$5{\cdot}2_3$	−962
3 : 3′-Dinitro- ,, [c]	$7{\cdot}72_9$	$0{\cdot}406_3$	0·057	$-43{\cdot}5_6$	404·4	63·8 [a]	$4{\cdot}0_5$	−861

[a] Calc. from $_{\infty}P_2$ for diphenyl by use of the R_G group values listed by Vogel, *J.*, 1948, 1833. [b] From Chau and Le Fèvre, *J.*, 1957, 2300. [c] Determinations in benzene. [d] From Le Fèvre and Vine, *J.*, 1938, 967.

Accordingly, if for the 2 : 2′- or 3 : 3′-dinitrodiphenyl we assume an azimuthal angle of χ^0 (such that $\chi = 0$ or 180° for the fully *cis*- or *trans*-arrangements of the C–NO_2 links), and write b_1^{dndp} (dndp = dinitrodiphenyl) as the polarisability in the direction of action of $\mu_{\text{resultant}}$, *i.e.*, along the bisector of the angle χ, and b_2^{dndp} as the polarisability parallel to the 4 : 1 : 1′ : 4′-line, we have, by transposing the values b_1, b_2, and b_3 for nitrobenzene:

$$b_1^{\text{dndp}} = 2[b_1 \cos^2 30 + b_2 \sin^2 30 - b^{\text{CH}}] \cos^2 \chi/2 + 2(b_3 - b^{\text{CH}}) \sin^2 \chi/2 + b_{\text{T}}^{\text{CC}}$$

$$b_2^{\text{dndp}} = 2[b_1 \cos^2 60 + b_2 \sin^2 60 - b^{\text{CH}}] + b_{\text{L}}^{\text{CC}}$$

$$b_3^{\text{dndp}} = 2[b_1 \cos^2 30 + b_2 \sin^2 30 - b^{\text{CH}}] \sin^2 \chi/2 + 2(b_3 - b^{\text{CH}}) \cos^2 \chi/2 + b_{\text{T}}^{\text{CC}}$$

Using $10^{23}b^{\text{CH}} = 0{\cdot}063_5$, $10^{23}b_{\text{L}}{}^{\text{CH}} = 0{\cdot}098_6$, and $10^{23}b_{\text{T}}{}^{\text{CC}} = 0{\cdot}027_4$ (*i.e.*, taking the C–C internuclear bond, in the absence of better knowledge of the effects of conjugation, as though it were single), we can compute the quantity $(2b_1 - b_2 - b_3)^{\text{dndp}}$, which enters the " dipole terms " of the dinitrodiphenyls, for various values of χ; it becomes algebraically negative when χ exceeds *ca.* 73°. Calculation also shows that for all these values of χ, θ_1 lies between 3 and 4×10^{-35}.

If now from the information obtained experimentally and listed in Table 2 under $_{\infty}({}_{m}K_2)$ and μ, the term $(\theta_1 + \theta_2)$ is deducted, and an allowance of 4×10^{-35} made for θ_1, then from θ_2, $(2b_1 - b_2 - b_3)$ emerges for 2 : 2′- and 3 : 3′-dinitrodiphenyl as $-0{\cdot}64 \times 10^{-23}$ and $-0{\cdot}94 \times 10^{-23}$ respectively. These figures when compared with our computed values for $(2b_1 - b_2 - b_3)$ correspond to the following specific values for χ: 2 : 2′-dinitrodiphenyl 92—93°, 3 : 3′-dinitrodiphenyl 101—102°. Such results resemble those previously obtained [4] from straightforward polarity considerations: the configurations are nearly orthogonal, with the azimuthal angle some 10° greater in the 3 : 3′- than in the 2 : 2′-isomer. Further, they illustrate once more the practicability of the method whereby b_1, b_2, and b_3 for a given structure can be predicted from link and group polarisabilities and used in the interpretation of experimental results.

Diphenyl and its 4-derivatives. By similar arguments the molar Kerr constants of diphenyl and its five *para*-derivatives can also be " synthesised " from available data (cf. ref. 12). For each of the six molecules the $_{\infty}({}_{m}K_2)$ expected for the flat configuration is greater than that for the orthogonal. Thus with diphenyl we expect:

	$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$	$10^{12}{}_{m}K_{\text{calc.}}$
Flat configuration	2·199	2·127	1·425	27·4
Orthogonal configuration	2·199	1·776	1·776	8·9

The value observed ($40{\cdot}5 \times 10^{-12}$) is larger than either of these ${}_{m}K$'s. The remaining five compounds exhibit the same disagreement:

Substituent:	4-F	4-Cl	4-Br	4-I	4-NO_2
$10^{12}\,{}_{m}K_{calc.}$	152	269	337	320	1869
$10^{12}\,{}_{\infty}({}_{m}K_{2})_{obs.}$	242	426	456	671	3265

(Only the calculated values for flat configurations are quoted, because those for $\chi = 90°$ are more distant still from those observed.) The ratios ${}_{m}K_{calc.}/{}_{m}K_{obs.}$ fall between 0·48 and 0·79.

The sum of the predicted semi-axes for diphenyl is $5{\cdot}751 \times 10^{-23}$, from which an electronic polarisation of 48·4 c.c. is calculable; the ${}_{E}P$ reported by Le Fèvre and Narayana Rao [13] is 49·5 c.c., giving $b_1 + b_2 + b_3 = 5{\cdot}886 \times 10^{-23}$. Parallel calculations for the other five molecules indicate a general deficiency throughout of *ca.* 1 c.c. in the electronic polarisations (taken as ${}_{D}P \times 0{\cdot}95$). When however the semi-axes are proportionately increased, the ${}_{m}K$'s computed for flat configurations are only brought slightly nearer the experimental values (*e.g.*, multiplication of the $10^{23}b$'s for diphenyl by 5·886/5·751 gives 2·251, 2·177, and 1·458, whence ${}_{m}K_{calc.}$ is $28{\cdot}8 \times 10^{-12}$). The cause of the lowness of ${}_{m}K_{calc.}$ (or the highness of ${}_{m}K_{expt.}$) must lie elsewhere.

The situation is understandable if diphenyl and its 4-derivatives have effectively flat configurations in solution. Spectroscopic evidence (occurrence of an intense absorption around 2500 Å with diphenyls unhindered in the *ortho*-positions, or forced into planarity as in fluorene) supports this.[14] Only in flat forms can ring-ring conjugation be strongly developed. Unpublished measurements (Bramley and Le Fèvre) on diarylpolyenes, together with data in refs. 10 and 12, show that molecular polarisability is notably enhanced in directions along which conjugation takes place. In terms of the present diphenyls, therefore, all the *a priori* estimates of b_1 are likely to be too small, and those of b_2 and b_3 too large; the greatest errors will probably (cf. ref. 12) be with the b_1's. Suppose, for the hydrocarbon, $10^{23}b_1 = 2{\cdot}4$, $10^{23}b_2 = 2{\cdot}1$, $10^{23}b_3 = 1{\cdot}4$, the total would be $5{\cdot}9 \times 10^{-23}$ (which is correct), and the expected ${}_{m}K$ would be $39\text{—}40 \times 10^{-12}$, in agreement with measurement. (With the same semi-axes an orthogonal configuration would give ${}_{m}K$ *ca.* 21×10^{-12}.) Like "adjustments" in the cases of the 4-derivatives produce similar results.

Attempts (by Purnachandra Rao) to test these remarks by determinations of depolarisation factors for the light scattered by carbon tetrachloride solutions of the 4-halogeno- and -nitro-diphenyls, and thus to ascertain b_1, b_2, and b_3 separately, have been defeated by fluorescence, which induced an excessively large apparent Δ (cf. refs. 10 and 12). Until a range of strong monochromatic light sources are available the subject cannot usefully be carried further. Evidently polarisability in the diphenyl series can be treated additively only when conjugation is absent, *i.e.*, when the species are non-planar.

UNIVERSITY OF SYDNEY, AUSTRALIA. [*Received, December 29th*, 1958.]

[13] Le Fèvre and Narayana Rao, *Austral. J. Chem.*, 1955, **8**, 39.
[14] Beaven, Hall, Lesslie, and Turner, *J.*, 1952, 854; *idem* and Bird, *J.*, 1954, 131; Everitt, Hall, and Turner, *J.*, 1956, 2286; Beaven and Hall, *J.*, 1956, 4637; Brawde and Forbes, *J.*, 1955, 3776.

XUM

535. *Molecular Polarisability. The Contributions of the Terms θ_1, θ_2, and θ_3 to the Kerr Constant of a Substance.*

By (Mrs.) C. G. Le Fèvre and R. J. W. Le Fèvre.

The molar Kerr constants of bromobenzene at infinite dilution in carbon tetrachloride have been determined at 25°, 35°, and 45°, to test a possible routine method for the separation of the anisotropy and dipole terms contributing to the ${}_mK$ of a polar solute. The temperature variation of the electric birefringence, measured as B, of five non-polar liquids has been examined for evidence of a temperature-independent term θ_3 in the ${}_mK$'s of such substances.

The "Kerr constant" B, measured as the difference between refractive indices parallel and perpendicular to an applied electric field E, can be deduced [1] *a priori* by the theory of Langevin, Born, and Gans for gaseous dielectrics and written as equation (2):

$$B = (n_p - n_s)/\lambda E^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$B = \frac{(n^2+2)^2}{3\lambda n} \cdot \frac{(\varepsilon+2)^2}{9} \cdot \frac{\pi N d}{M} (\theta_1 + \theta_2) \quad . \quad . \quad . \quad . \quad (2)$$

Symbols have conventional meanings; θ_1 and θ_2 are the "anisotropy" and "dipole" terms, expansions of which are given in refs. 1 and 2; these include the semi-axes of the molecular electro-optical polarisability ellipsoid and the resolutes of the molecular resultant dipole moment along the directions in the molecule corresponding to the said semi-axes. Stereochemical problems, which can be solved through polarisability considerations, necessitate a knowledge of the magnitudes of these semi-axes, so we need three equations from which they can be extracted. If θ_1 and θ_2 can be separated from eqn. (2), the introduction of eqn. (3) often completes the requisite information.

$$\text{Electronic polarisation} = {}_EP = 4\pi N(b_1 + b_2 + b_3)/9 \quad . \quad . \quad . \quad (3)$$

Stuart and Volkmann,[3] using extant values of K (*i.e.*, $B\lambda/n$) and their own observations on organic substances well above the normal boiling points, evaluated polarisability ellipsoid semi-axes for about thirty compounds, θ_1 being computed from depolarisation factors for light scattered by the vapours (see refs. 1—3 for equations).

We have [1,4a,4b] developed a technique and extrapolation procedure for determining the specific or molar Kerr constant ${}_\infty({}_mK_2)$ of a solute at infinite dilution in a solvent; these quantities follow if the refractive indices n_p and n_s in eqn. (1) are replaced by the corresponding specific or molecular refractions. The molar Kerr constant contains the sum $\theta_1 + \theta_2$ (see eqn. 4):

$${}_mK = 2\pi N(\theta_1 + \theta_2)/9 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and by illustrating that ${}_mK$'s from gases or solutions were similar, we extended [4] the applicability of the Kerr effect to soluble solids and involatile materials.

At the time the paucity and validity of available depolarisation factors severely limited the complete analysis of molecular polarisability, and alternative sources of information were sought (see ref. 1, p. 287 for summary, also refs. 4*b* and 4*c*); these were regarded as speculative and unsatisfactory.

Accordingly we tried to separate θ_1 from θ_2 by using their different temperature dependences. Bromobenzene was chosen, and its molar Kerr constants measured at

[1] Le Fèvre and Le Fèvre, *Rev. Pure Appl. Sci.*, 1955, **5**, 261.
[2] Le Fèvre and Purnachandra Rao, *J.*, 1957, 3644.
[3] Stuart and Volkmann, *Ann. Physik*, 1933, **18**, 121.
[4] Le Fèvre and Le Fèvre, (*a*) *J.*, 1953, 4041, (*b*) *J.*, 1954, 1577 (*c*) *J.*, 1955, 1641, 2750.

XUM

infinite dilution in carbon tetrachloride at 25°, 35°, and 45°; results and ${}_{\infty}({}_{m}K_2)$'s obtained are in Tables 1 and 2. Nevertheless, the tedium and technical difficulties thus involved at higher temperatures led us to wait while Le Fèvre and Purnachandra Rao tried to determine molecular anisotropy by light scattering, which they have now done.[2]

TABLE 1. *Kerr effects, refractive indices, densities, and dielectric constants for solutions of bromobenzene in carbon tetrachloride.**

10^5w_2	$10^7\Delta B$	$(n)_{12}$	$(d_4^t)_{12}$	$\varepsilon_{12}{}^t$	10^5w_2	$10^7\Delta B$	$(n)_{12}$	$(d_4^t)_{12}$	$\varepsilon_{12}{}^t$
Temperature = 25°					Temperature = 25°				
0	—	1·4575	1·5845	2·2270	2411	0·254	1·4600	1·5822	2·3015
806	0·085	—	1·5837	2·2534	2599	0·285	1·4603	1·5820	2·3068
1122	0·118	1·4587	1·5835	2·2615	2664	0·291	1·4604	1·5818	2·3083
1398	0·143	—	1·5832	2·2698	3114	0·338	1·4607	1·5812	2·3220
1700	0·182	1·4594	1·5827	2·2795					

whence $10^7\Delta B = 10{\cdot}19w_2 + 23{\cdot}6w_2{}^2$; $\Sigma(n_{12} - n_1)/\Sigma w_2 = 0{\cdot}106_5$; $\Sigma(d_{12} - d_1)/\Sigma w_2 = -0{\cdot}0993$; $\Sigma(\varepsilon_{12} - \varepsilon_1)/\Sigma w_2 = 3{\cdot}08$.

Temperature = 35°					Temperature = 35°				
0	—	1·4519	1·5651	2·2092	1681	0·152	1·4536	1·5638	2·2581
1333	0·126	—	1·5641	2·2472	2297	0·219	1·4542	1·5634	2·2770
1398	0·135	—	1·5641	2·2503	2411	0·224	1·4543	1·5633	2·2792
1584	0·146	—	1·5639	2·2552	3904	0·354	1·4557	1·5626	2·3243
1631	0·147	1·4535	1·5638	2·2567					

whence $10^7\Delta B = 9{\cdot}51w_2 - 10{\cdot}6w_2{}^2$; $\Sigma(n_{12} - n_1)/\Sigma w_2 = 0{\cdot}0990$; $(\Sigma d_{12} - d_1)/\Sigma w_2 = -0{\cdot}0788$; $\Sigma(\varepsilon_{12} - \varepsilon_1)/(\Sigma w_2 = 2{\cdot}92$.

Temperature = 45°					Temperature = 45°				
0	—	1·4460	1·5458	2·1873	4973	0·440	1·4507	1·5430	2·3254
1378	0·119	1·4473	1·5450	2·2253	6363	0·546	1·4522	1·5422	2·3636
2131	0·186	1·4480	1·5446	2·2462	6461	0·546	1·4523	1·5421	2·3673
2526	0·255	1·4484	1·5444	2·2571	7215	0·624	1·4530	1·5417	2·3882
4271	0·332	1·4501	1·5434	2·3053	13758	1·211	1·4594	1·5378	2·5716

whence $10^7\Delta B = 8{\cdot}46w_2 + 2{\cdot}38w_2{}^2$; $\Sigma(n_{12} - n_1)/\Sigma w_2 = 0{\cdot}096_4$; $\Sigma(d_{12} - d_1)/\Sigma w_2 = -0{\cdot}0570_4$; $\Sigma(\varepsilon_{12} - \varepsilon_1)/\Sigma w_2 = 2{\cdot}78$.

* Headings: w_2 = weight fraction of solute in solution, ΔB = increment in Kerr constant from solvent to solution, n = refractive index for Na light, d = density, ε = dielectric constant; subscripts 1, 2, and 12, denote solvent, solute, and solution respectively; for $B_1{}^t$ when $w_2 = 0$ see Table 3.

TABLE 2. *Calculation * of molar Kerr constants at infinite dilution in carbon tetrachloride.*

						Solvent constants used		
Temp.	$\alpha\varepsilon_1$	β	γ	δ	$10^{12}\ {}_{\infty}({}_{m}K_2)$	H	J	$10^{17}({}_{s}K_1)$
25°	3·10	−0·075	0·073	145·6	170·7	2·060	0·4731	749
35	2·92	−0·050	0·068	137·8	163·4	2·053	0·4751	757
45	2·78	−0·037	0·067	126·3	149·3	2·044	0·4776	755

* For explanation of symbols and method of calculation, see p. 283 of ref. 1.

Anisotropy and Dipole Terms for Bromobenzene.—From ${}_{\infty}({}_{m}K_2)$ (Table 2) the sums $(\theta_1 + \theta_2)_t$ follow as 40·59, 38·86, and 35·50 (all $\times 10^{-35}$). By writing the temperature-invariant parts of θ_1 and θ_2 as

$$C_1 = (b_1 - b_2)^2 + (b_2 - b_3)^2 + (b_3 - b_1)^2,$$

and $$C_2 = \mu^2(2b_1 - b_2 - b_3)$$

we have generally:

$$(\theta_1 + \theta_2)_T = [({}_{D}PC_1/{}_{E}P)/45kT] + C_2/45k^2T^2$$

where T = temperature in °K and ${}_{D}P/{}_{E}P$ = distortion polarisation ÷ electronic polarisation = 1·091 for bromobenzene.[4b] Solutions of the consequent simultaneous equations are unsatisfactory: between 298° and 318° K, C_1 has a small negative value, while between

298° and 308° K, C_1 is $4{\cdot}7 \times 10^{-46}$ and C_2 is $10{\cdot}0 \times 10^{-60}$. Presumably wider temperature ranges and more observations would give better results, but this would be unsuitable for a *routine* procedure.

The temperature method is inadequate for our purpose because the difference between $\theta_1 + \theta_2$ for two temperatures is relatively small and liable to contain the errors of two much larger numbers. That the individual ${}_\infty({}_mK_2)$ measurements are not seriously incorrect can be demonstrated, because we now know [5] that C_1 should be $0{\cdot}94 \times 10^{-46}$ and C_2 $26{\cdot}74 \times 10^{-60}$; therefore $10^{12}\ {}_mK_{calc.}$ for 298°, 308°, and 318° K should be 171, 161, and 151, against 171, 163, and 149 recorded: the discrepancies, *ca.* 1·3%, are of the order sometimes experienced among repeated measurements of ${}_\infty({}_mK_2)$. (This study of the bromobenzene–carbon tetrachloride system is the first attempt to check by experiment the influence of temperature on the molar Kerr constant of a solute at infinite dilution.)

Temperature-independent Component of the Molar Kerr Constant.—We considered the possible existence of a temperature-invariant term (denoted [1,6] by θ_3) in the right-hand side of eqns. (2) and (4). According to classical theory the differences $(b_1 - b_2)$, $(b_2 - b_3)$, and $(b_3 - b_1)$ for tetrahedral molecules (*e.g.*, CCl_4, CH_4,CBr_4) should be zero, and neither finite Kerr effects nor depolarisation factors should be displayed. In fact, small values for both these properties are observed.

It was shown,[6] *a priori*, that the apparent molar Kerr constant of a structure CX_4 might arise from distortion of the molecule by the applied electrostatic field; this could be part of the mechanism of the hyperpolarisability induced at high field strengths discussed by Coulson, Maccoll, and Sutton.[7] Alternatively, Buckingham and Pople [8] considered such non-zero values for ${}_mK$ to be due to second-order effects from a curved relationship between molecular polarisability and field strength.

Whatever its origin, the negligibility or otherwise of the contribution of θ_3 to ${}_mK$ of an anistropic molecule would obviously be important in stereochemical applications of the Kerr effect. This was noted in ref. 1 (p. 309. Correction: the equation in para. 8·1 should have 9 as a denominator) where we discussed the relative magnitudes of θ_3 in tetrahedral and centrosymmetric molecules; experimentally, for a non-polar liquid, ${}_mK = 2\pi N(\theta_1 + \theta_3)/9$ and only θ_1 is temperature-dependent; hence a plot of ${}_mK_T$ against $1/T$, by extrapolation to $1/T = 0$, should yield $2\pi N\theta_3/9$. Examples are reported below.

Carbon tetrachloride. The temperature-variation of its Kerr constant B (fundamental to our whole programme) appears never to have been examined. Table 3 contains results now obtained, together with other information leading to the apparent molar Kerr constants.

TABLE 3. *Apparent molar Kerr constants of carbon tetrachloride between* 20° *and* 45°.

t (°C)	d_4^t	n_D^t	ε^t	10^7B	$10^{12}({}_mK_{liq.})$
20	1·5940	1·4604	2·2360	0·072	$1{\cdot}1_7$
25	1·5845	1·4575	2·2270	0·070	$1{\cdot}1_5$
35	1·5651	1·4519	2·2092	0·069	$1{\cdot}1_6$
40	1·5557	1·4493	2·2003	0·068	$1{\cdot}1_6$
45	1·5458	1·4460	2·1873	0·067	$1{\cdot}1_6$

Within experimental limits set by the small B's, the ${}_mK$'s are unaffected by temperature, as expected if the apparent molar Kerr constant contains only the temperature-independent term θ_3 and other constants.

Carbon disulphide, mesitylene, benzene, p-*xylene, and tetrachloroethylene.* Buckingham and Raab [9] used values of B/temperature given by Lyon and Wolfram [10] for carbon

[5] Le Fèvre and Purnachandra Rao, *J.*, 1958, 1465.
[6] Le Fèvre, Le Fèvre, and Narayana Rao, *J.*, 1956, 708.
[7] Coulson, Maccoll, and Sutton, *Trans. Faraday Soc.*, 1952, **48**, 106.
[8] Buckingham and Pople, *Proc. Phys. Soc.*, 1955, **68**, *A*, 905.
[9] Buckingham and Raab, *J.*, 1957, 2341.
[10] Lyon and Wolfram, *Ann. Physik*, 1920, **63**, 739.

disulphide, and Grodde's four figures [11] for mesitylene, to estimate theoretically the temperature-independent parts of ${}_{\mathrm{m}}K$. Having obtained results for some non-polar liquids (including mesitylene, values for which differed from Grodde's), and having noted that data in the literature for carbon disulphide did not agree, we considered (with Dr. A. D. Buckingham) that all observations merited repetition; this has now been done, except for carbon disulphide (see Table 4).

Owing to lack of facilities for low-temperature work, carbon disulphide was not studied. A fairly large number of B *versus* t data are available from Leiser [12] (14° to 28°), Lyon and Wolfram [10] (−78° to 18°), Bergholm [13] (−20° to 41·5°), and Kurten [14] (2° to 38°); these, in

TABLE 4. *Temperature-dependence of* ${}_{\mathrm{m}}K_{\mathrm{liq.}}$.

t (°c)	d_4^t	n^t	ε_t	10^7B_t	$10^{12}({}_{\mathrm{m}}K_t)_{\mathrm{obs.}}$	$10^{12}({}_{\mathrm{m}}K_t)_{\mathrm{calc.}}$
			Benzene			
15	0·8842	1·5044	$2·292_5$	0·423	$5·9_4$	$5·9_6$
20	0·8790	1·5010	$2·282_5$	0·412	$5·8_6$	$5·8_8$
25	0·8738	1·4979	$2·272_5$	0·401	$5·7_{75}$	$5·7_8$
30	0·8684	1·4949	2·263	0·390	$5·6_9$	$5·6_8$
35	0·8612	1·4907	2·254	0·379	$5·6_2$	$5·5_8$
40	0·8576	1·4876	2·243	0·368	$5·5_2$	$5·4_9$
45	0·8529	1·4851	2·233	0·356	$5·4_0$	$5·4_2$
50	0·8466	1·4811	2·223	0·345	$5·3_{15}$	$5·3_2$
55	0·8400	1·4776	2·213	0·334	$5·2_8$	$5·2_3$
60	0·8359	1·4744	$2·203_5$	0·324	$5·1_3$	$5·1_5$
65	0·8299	1·4720	$2·193_5$	0·314	$5·0_4$	$5·0_7$
	whence $10^{12}({}_{\mathrm{m}}K_t) = -0·1_5 + 1766/T$; standard error in constant term, $\pm 0·1_8$.					
			p-Xylene			
15	$0·8653_5$	1·4984	2·278	0·740	$14·5_8$	$14·7_4$
20	0·8610	1·4958	2·270	0·727	$14·4_8$	$14·5_2$
25	$0·8566_5$	1·4932	2·262	0·710	$14·3_0$	$14·3_2$
30	0·8523	1·4906	2·254	0·695	$14·1_4$	$14·1_2$
35	$0·8480_5$	1·4880	2·246	0·680	$13·9_9$	$13·9_2$
40	0·8436	1·4854	2·238	0·662	$13·7_7$	$13·7_4$
45	$0·8392_5$	1·4828	2·230	0·650	$13·6_7$	$13·5_9$
50	0·8349	1·4802	2·222	0·637	$13·5_4$	$13·3_8$
55	$0·8305_5$	1·4776	2·214	0 616	$13·2_4$	$13·2_1$
60	0·8262	1·4750	2·206	0·605	$13·1_4$	$13·0_4$
65	$0·8218_5$	1·4724	2·198	0·588	$12·9_3$	$12·8_8$
70	0·8175	1·4698	2·190	0·573	$12·7_3$	$12·7_2$
75	$0·8131_5$	1·4672	2·182	0·559	$12·4_9$	$12·5_7$
80	0·8088	1·4646	2·174	0·545	$12·3_7$	$12·4_3$
85	$0·8054_5$	1·4620	2·166	0·530	$12·1_5$	$12·2_8$
	whence $10^{12}({}_{\mathrm{m}}K_t) = 2·1_7 + 3620/T$; standard error in constant term, $\pm 0·2_5$.					
			Mesitylene			
15	0·8678	1·5021	2·279	0·760	$16·8_5$	$17·3_0$
20	0·8637	1·4998	2·270	0·748	$16·7_{45}$	$17·0_0$
25	0·8596	1·4975	2·263	$0·725_5$	$16·4_3$	$16·7_2$
30	0·8557	1·4952	2·256	$0·703_5$	$16·0_7$	$16·4_3$
35	0·8512	1·4929	2·249	0·692	$15·9_8$	$16·1_5$
40	0·8476	1·4906	2·241	0·681	$15·8_7$	$15·8_8$
45	0·8429	1·4883	2·233	$0·666_5$	$15·7_1$	$15·6_8$
50	0·8393	1·4859	2·225	0·650	$15·4_7$	$15·3_7$
55	0·8341	1·4836	2·216	0·634	$15·2_8$	$15·1_3$
60	0·8310	1·4813	2·207	0·620	$15·0_8$	$14·9_0$
65	0·8253	1·4790	2·198	0·604	$14·8_6$	$14·6_7$
70	0·8209	1·4767	2·189	0·584	$14·5_6$	$14·4_4$
75	0·8158	1·4744	2·181	0·571	$14·4_9$	$14·2_3$
80	0·8119	1·4721	2·172	0·556	$14·1_7$	$14·0_2$
85	0·8074	1·4698	2·164	0·543	$14·0_0$	$13·8_2$
	whence $10^{12}({}_{\mathrm{m}}K_t) = -0·5_1 + 5130/T$; standard error in constant term, $\pm 0·4_2$.					

[11] Grodde, *Physikal. Z.*, 1938, **39**, 772.
[12] Leiser, "Elektrische Doppelbrechung der Kohlenstoff Verbindungen," Abh. Deut. Bunsen Gesellschaft, No. 4, Halle a.S., 1910.
[13] Bergholm, *Ann. Physik*, 1921, **65**, 128.
[14] Kurten, *Physikal. Z.*, 1931, **32**, 251.

XUM

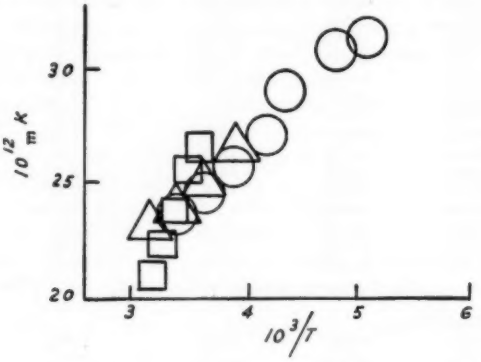
TABLE 4. (*Continued.*)

t (°c)	d_4^t	n^t	ε_t	$10^7 B_t$	$10^{12}({}_mK_t)_{obs.}$	$10^{12}({}_mK_t)_{calc.}$
			Tetrachloroethylene			
15	1·63109	1·5078	2·32	0·820	$15·2_2$	$15·4_7$
20	1·62285	1·5053	2·31	0·788	$14·7_9$	$14·9_4$
25	1·61461	1·5028	2·30	0·765	$14·5_3$	$14·6_8$
30	1·60637	1·5003	2·29	0·748	$14·3_7$	$14·4_3$
35	1·59813	1·4978	2·28	0·729	$14·1_7$	$14·2_9$
40	1·58989	1·4953	2·27	0·712	$14·0_0$	$13·9_7$
45	1·58165	1·4928	2·26	0·693	$13·7_9$	$13·7_9$
50	1·57341	1·4903	2·25	0·674	$13·5_7$	$13·5_2$
55	1·56517	1·4878	2·24	0·658	$13·4_1$	$13·3_1$
60	1·55693	1·4853	2·23	0·645	$13·3_0$	$13·1_1$
65	1·54869	1·4828	2·22	0·625	$13·0_4$	$12·9_1$
70	1·54045	1·4803	2·21	0·604	$12·7_5$	$12·7_2$
75	1·53221	1·4778	2·20	0·583	$12·4_6$	$12·5_3$
80	1·52397	1·4753	2·19	0·564	$12·2_0$	$12·3_5$
85	1·51573	1·4728	2·18	0·545	$11·9_3$	$12·1_7$

whence $10^{12}({}_mK_t) = -0·30 + 4465/T$; standard error in constant term, $\pm 0·6_1$.

Dielectric constants were obtained from " Tables of Dielectric Constants of Pure Liquids," Maryott and Smith, Nat. Bur. Stand. Circular No. 514 (1951), except for mesitylene for which data were interpolated from Grodde's figures. Densities and refractive indexes (Na_D) were from Timmermans, " Physico-chemical Constants of Pure Organic Compounds," Elsevier, New York, 1950, or Egloff, " Physical Constants of Hydrocarbons," Vol. III, Amer. Chem. Soc. Monographs, Reinhold, New York, 1946, pp. 88, 89.

conjunction with density, refractive index, etc., values, are shown as molar Kerr constants in the Figure. The points do not lie on a single straight line, but roughly in a corridor;



Plot of ${}_mK$ for CS_2 against the reciprocal of absolute temperature.
○ Lyon and Wolfram.
△ Bergholm.
□ Kurten.

their scatter is such that the possibility that ${}_mK$ for CS_2 is negligible at very high temperatures is by no means eliminated. The other substances, except *p*-xylene, appear to have near-zero θ_3 terms. For *p*-xylene the temperature-independent part of ${}_mK$ is *ca.* 2×10^{-12}; this is surprising in comparison with the results for benzene and mesitylene and cannot readily be explained without questioning our observations of B and those for n, d_4^t, etc., which are from the literature. Even so, 2×10^{-12} is only one seventh of the ${}_mK$ of *p*-xylene at ordinary temperatures.

Conclusions.—(1) For a polar solute θ_1 and θ_2 cannot be found separately by measuring the temperature coefficient of ${}_\infty({}_mK_2)$, thus avoiding recourse to light-scattering, sufficiently precisely with present apparatus over a convenient temperature range.

(2) Measurements at 25° involving light scattering give ${}_\infty({}_mK_2)$ of bromobenzene at 35° and 45° within 1·3% of the values found.

(3) The apparent molar Kerr constant of carbon tetrachloride, being invariant with temperature, is wholly due to θ_3

(4) Anisotropic molecules may have ${}_mK$'s containing θ_1, θ_2, and θ_3, where in general

$\theta_2 > \theta_1 > \theta_3$. When the molecule is non-polar, $\theta_2 = 0$. For benzene, mesitylene, and tetrachloroethylene, θ_3 appears to be near zero; for *p*-xylene it may cause *ca.* 15% of the observed molar Kerr constant; for carbon disulphide the situation is indefinite.

Experimental

The apparatus used with the bromobenzene–carbon tetrachloride mixtures was as previously [4a] described apart from small modifications to the cell. An extra tube, admitting a thermometer readable to 0·1° to the liquid, was added parallel and close to the inlet (*I* in Fig. 2 of ref. 4*a*). The ends of the cell body were ground plane and polished, so that optically flat fused-silica end-plates made liquid-tight closure by gentle contact. The end-plates were selected to have less inherent strain than that measured as $10^{-6}\lambda$. They were held in position by Polythene film covers, suitably pierced for the light to pass, the "skirts" being secured around the cell by rubber bands; brass rings cemented near the cell ends prevented slipping. This minimised pressure on the end-plates, and eliminated strains due to warming of metal end-caps or to swelling of washers through absorption of liquids. The quartz plates did not develop detectable strain on heating to 45°.

The cell was supported, well inside an asbestos-cement air-oven, on a cradle [4a] having a slow-motion adjustment so that the cell could be moved vertically to centralise the light-path between the electrodes; such compensation of the thermal expansion of the metal pillars proved essential. The lower parts of the inside walls of the oven carried heating tapes fed through a Variac transformer; uniformity of temperature was maintained by a small vibration-free fan. Control was checked to ensure that all temperatures in the oven and cell were the same within 0·1°.

Above *ca.* 60° the Polythene and rubber bands became unreliable, and the risk of thermal strains' appearing in the end-plates increased. The first difficulty was met by replacing the ground ends of the cell with accurately fitted B.24 Pyrex sockets, in which two fused-silica B.24 cones, to whose smaller ends optically-plane silica discs had been sealed and well annealed, were held lightly by springs running between lugs. It was necessary to increase by grinding the clearance between cone and socket for about 0·5 in. behind the optical flat to avoid strain on the end-plate due to the springs or creep of the liquid, particularly at higher temperatures.

Strains in the end-plates, being liable to appear unpredictably, are a major problem in measurements of the Kerr effect. Even if (as is unlikely) the strains in the end-plates were uniformly along diameters, so that their net effect would be that of a uniaxial crystal, one would not know where the principal axes of that crystal lay. If therefore this effect were appreciable, the slightest relative movement of cell and light-path would change it, and determinations of B (particularly if small) could be invalidated. The only precaution possible, since the polariser is in a fixed azimuth of 45°, is to rotate the cell through 45° about its long axis and to search the optical field with a Brace compensator; this procedure should ensure the absence of mechanical strains.

Several further factors need care. It is assumed that the light pencil is incident normally on both end-plates. However, even for the fused-silica plates, if the light does not fall normally on the plate nearer the polariser, refraction by the dielectric results in the beam striking the other end-plate at an angle α out of the normal, and by means of the Brace compensator the phase difference δ arising from this non-normal transmission of the light can be measured. If now the electric field E is applied, orientation of the molecules changes the refractive index of the liquid, and α will become α' and have associated with it a phase difference δ'; δ' is included in the phase difference Δ observed for the dielectric plus cell, but because $\delta' \neq \delta$, the phase difference due solely to the Kerr effect cannot be obtained by subtracting δ from Δ. There is no method of determining δ', which alters with E. The apparatus should therefore be aligned, and end-plates be selected, so that the position of the light spot seen through the observer's telescope is unchanged by the electric field. If all components are correctly arranged, the same value of B_{liquid} is obtained by the use of different voltages.

University of Sydney, New South Wales,
Australia.

[*Received, January 26th*, 1959.]

XUM

536. *Chromones and Flavones. Part I. Iodination of 5- and 7-Hydroxy-2-methylchromone.*

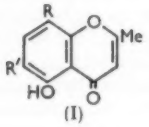
By M. V. Shah and Suresh Sethna.

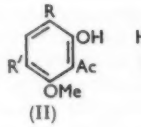
Iodination of 5- or 7-hydroxy-2-methylchromone gave the 8-iodo- or 6 : 8-di-iodo-derivatives.

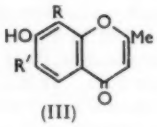
Offe [1] iodinated 2-methylchromone and obtained 2-iodomethylchromone. No other work on the iodination of chromones has been reported. In the present paper iodination of 5- and 7-hydroxy-2-methylchromone with iodine and iodic acid or, less well, with iodine and ammonia and with iodine monochloride is described.

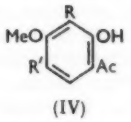
5-Hydroxy-2-methylchromone (Ia) on iodination with the theoretical amount of iodine and iodic acid ($5RH + 4I + HIO_3 \longrightarrow 5RI + 3H_2O$) gave the 8-iodo-derivative (Ib). On nitration it gave a compound identical with the iodination product of 5-hydroxy-2-methyl-6-nitrochromone; its methyl ether, on hydrolysis, gave an iodo-ketone different from that obtained by iodination of 2-hydroxy-6-methoxyacetophenone, but the derived methyl ethers were identical. The iodo-ketone obtained in hydrolysis therefore has structure (IIb) and that one obtained by direct iodination has structure (IId).

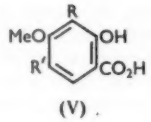
With twice the above amounts of reagents 5-hydroxy-2-methylchromone gave the 6 : 8-di-iodo-derivative (Ic). Its methyl ether on hydrolysis gave the 3 : 5-di-iodo-ketone (IIc) which was identical with the iodination product of 2-hydroxy-6-methoxyacetophenone.


(I)


(II)


(III)


(IV)


(V)

	a	b	c	d	e
R	H	I	I	H	I
R′	H	H	I	I	OH

7-Hydroxy-2-methylchromone (IIIa), as above, gave first the 8-iodo-derivative (IIIb). Its methyl ether on hydrolysis gave an iodo-ketone and an iodo-acid, both of which underwent Elbs persulphate oxidation smoothly, suggesting that the *para*-position to the hydroxyl group must be free.[2] The hydrolysis products therefore have the 3-iodo-structures (IVb and Vb respectively), and the oxidation products are (IVe) and (Ve) respectively. The same iodo-ketone (IVb) was obtained on direct iodination of peonol.

With three times amounts of iodine and iodic acid 7-hydroxy-2-methylchromone gave the 6 : 8-di-iodo-derivative (IIIc). Its methyl ether on hydrolysis gave a di-iodo-acid, and a di-iodo-ketone identical with that obtained on the iodination of peonol. The di-iodo-acid, on Elbs persulphate oxidation, lost one iodine atom and gave the acid (Ve) obtained as above. The methyl ether of the di-iodo-acid was identical with the product obtained on methylation of the iodination product of β-resorcylic acid.

The di-iodochromone (IIIc), on prolonged heating in acetic acid, lost one iodine atom and gave a mono-iodochromone which must be the 6-iodo-derivative (IIId) as it was different from (IIIb). Its methyl ether on hydrolysis gave a monoiodo-ketone (IVd) and a monoiodo-acid (Vd) different from (IVb) and (Vb). The same iodo-ketone (IVd) was obtained on iodination of peonol with iodine and ammonia. The iodo-ketone, on Elbs persulphate oxidation, lost iodine and gave 2 : 5-dihydroxy-4-methoxyacetophenone.[3]

With iodine and ammonia or iodine monochloride as iodinating agents similar results

[1] Offe, *Ber.*, 1938, **71**, 1837.
[2] Baker and Brown, *J.*, 1948, 2303.
[3] Bargellini and Aureli, *Atti Accad. Lincei*, 1911, **20**, 118.

were obtained except that the di-iodo-compound from 7-hydroxy-2-methylchromone could not be obtained.

No tri-iodo-derivative could be obtained from either chromone, even with excess of the iodinating agents.

The methyl ethers of the chromones (Ia) and (IIIa) could not be iodinated. Iodine monochloride gave chloro-compounds.

Iodination of resacetophenone was also examined. Segalle,[4] using potassium iodate and potassium iodide in acetic acid, obtained a monoiodo-compound to which no definite structure was assigned. This must be the 3-iodo-derivative as its dimethyl ether was identical with the methyl ether of (IVb). Use of ammonia and iodine, however, gave the 5-iodo-derivative, whose dimethyl ether was identical with the methyl ether of (IVd) described above. Use of double the quantity of the iodinating agent gave the 3 : 5-di-iodo-ketone whose dimethyl ether was identical with the methyl ether of (IVc).

Experimental

Iodinations (*see Table* 1).—(A) *With iodine and iodic acid.* The substance (0·01 mole) was dissolved in the minimum quantity of warm alcohol, and the required quantities of iodine and iodic acid (in water) were added. The mixture was stirred for 2 hr. at room temperature and the iodo-derivative, which separated from the solution or on dilution with water, was crystallised from acetic acid.

Table 1.

No.	Compound	Method	Product	M. p.[a]	Yield (%)[b]	Formula	Found I (%)	Reqd. I (%)
1	5-Hydroxy-2-methylchromone	A, B, C	8-Iodo-	171°	49	$C_{10}H_7O_3I$	42·4	42·1
		A, B, C	6 : 8-Di-iodo-	238	52	$C_{10}H_6O_3I_2$	59·7	59·3
2	7-Hydroxy-2-methylchromone	A, B, C	8-Iodo-	213	47	$C_{10}H_7O_3I$	42·5[c]	42·1
		A	6 : 8-Di-iodo-	212	58	$C_{10}H_6O_3I_2$	59·8	59·3
3	2-Hydroxy-6-methoxyacetophenone	A, B, C	5-Iodo-	116	68	$C_9H_9O_3I$	43·7	43·5
		A, B, C	3 : 5-Di-iodo-	111	76	$C_9H_8O_3I_2$	60·4	60·8
4	2-Hydroxy-4-methoxyacetophenone	A	3-Iodo-	152	15	$C_9H_9O_3I$	43·8	43·5
		B	5-Iodo-	161	13	$C_9H_9O_3I$	42·9	43·5
		A, B, C	3 : 5-Di-iodo-	98—99	8	$C_9H_8O_3I_2$	61·2	60·8
5	2 : 4-Dihydroxyacetophenone	A	3-Iodo-	164	82	$C_8H_7O_3I$	45·5	45·7
		B	5-Iodo-	184	15	$C_8H_7O_3I$	45·8	45·7
		A, B, C	3 : 5-Di-iodo-	180	86	$C_8H_6O_3I_2$	63·0	62·9
6	2 : 4-Dihydroxybenzoic acid	A, B, C	3 : 5-Di-iodo-	218[d]	70	$C_7H_4O_4I_2$	62·9	62·8

Completely methylated products of the iodo-compound

No.	M. p.	Formula	Found (%) C	Found (%) H	Found (%) I	Required (%) C	Required (%) H	Required (%) I
1	92—95°	$C_{11}H_9O_3I$	41·7	2·8	39·8	41·8	2·8	40·2
	207—208	$C_{11}H_8O_3I_2$	30·0	1·9	57·4	29·9	1·8	57·5
2	191—192	$C_{11}H_9O_3I$	41·9	2·8	40·8	41·8	2·8	40·2
	162	$C_{11}H_8O_3I_2$	30·2	1·7	57·7	29·9	1·8	57·5
3	71—72	$C_{10}H_{11}O_3I$	38·6	3·7	41·3	39·2	3·6	41·5
	—	—	—	—	—	—	—	—
4	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—
5	101—102	$C_{10}H_{11}O_3I$	39·5	3·6	41·8	39·2	3·6	41·5
	145	$C_{10}H_{11}O_3I$	39·1	3·8	41·5	39·2	3·6	41·5
	59—60	$C_{10}H_{10}O_3I_2$	27·7	2·4	59·2	27·8	2·3	58·8
6	183—184	$C_9H_8O_4I_2$	25·0	1·9	58·6	24·9	1·8	58·6

[a] Some of the hydroxy-iodo-derivatives decompose 20—30° below their m. p.s and melt finally at the above temperatures. [b] Yields are those obtained by method A. [c] After drying *in vacuo* at 110° for 3 hr. [d] Nicolet and Sampey (*J. Amer. Chem. Soc.*, 1927, **49**, 1796) report m. p. 193—196° (decomp.).

(B) *With iodine and ammonia.* To the substance (0·01 mole), dissolved in 22% aqueous ammonia (40 ml.), a solution of iodine in potassium iodide in required quantity was added with stirring at room temperature during ½ hr. The mixture was stirred for a further 2 hr. then

[4] Segalle, *Monatsh.*, 1896, **17**, 314.

poured into excess of dilute ice-cold sulphuric acid. The precipitate was recrystallised from acetic acid. In the iodination of 5-hydroxy-2-methylchromone a mixture of dioxan and ammonia was used. In the case of 2 : 4-dihydroxyacetophenone the iodine solution was added within ½ hr. and the mixture immediately acidified.

(C) *With iodine monochloride.* To the substance (0·01 mole), dissolved in the minimum quantity of acetic acid or alcohol, hydrochloric acid (*d* 1·11; 15 ml.) was added. The mixture was then added to the requisite amount of iodine monochloride and kept for 24 hr. at 50°. The mixture was worked up as usual.

Preparation of Methyl Ethers.—The iodo-derivatives were methylated by refluxing their acetone solutions with dimethyl sulphate in presence of anhydrous potassium carbonate.

Hydrolysis of Iodochromones.—Hydrolysis by boiling 10% sodium hydroxide solution gave the results shown in Table 2.

TABLE 2. *Hydrolysis products of the iodochromones.*

2-Methyl-chromone	Products [a]	M. p.	Formula	Found (%) C	H	I	Required (%) C	H	I
8-Iodo-5-methoxy	2-Hydroxy-3-iodo-6-methoxy-acetophenone	57°	$C_9H_9O_3I$	36·9	3·1	43·4	37·0	3·1	43·5
6 : 8-Di-iodo-5-methoxy	2-Hydroxy-3 : 5-di-iodo-6-meth-oxyacetophenone	—	—	—	—	—	—	—	—
8-Iodo-7-methoxy	(1)2-Hydroxy-3-iodo-4-methoxy-acetophenone	—	—	—	—	—	—	—	—
	(2)2-Hydroxy-3-iodo-4-methoxy-benzoic acid	218 [b]	$C_8H_7O_4I$	33·0	2·5	43·5	32·6	2·4	43·2
6-Iodo-7-methoxy	(1)2-Hydroxy-5-iodo-4-methoxy-acetophenone	—	—	—	—	—	—	—	—
	(2)2-Hydroxy-5-iodo-4-methoxy-benzoic acid	245 [b]	$C_8H_7O_4I$	32·9	2·3	42·9	32·6	2·4	43·2
6 : 8-Di-iodo-7-methoxy	(1)2-Hydroxy-3 : 5-di-iodo-4-methoxyacetophenone [b]	—	—	—	—	—	—	—	—
	(2)2-Hydroxy-3 : 5-di-iodo-4-methoxybenzoic acid	217 [b]	$C_8H_6O_4I_2$	22·6	1·2	61·1	22·9	1·4	60·5

[a] For acetophenones see Table 1. [b] With effervescence.

5-Hydroxy-8-iodo-2-methyl-6-nitrochromone.—The iodo-chromone (Ib) (1 g.) was dissolved in glacial acetic acid (40 ml.) and cooled below 10°. Nitric acid (*d* 1·42; 10 ml.) was added dropwise with stirring. The mixture was added to ice after 24 hr. and the precipitate crystallised from acetic acid in thick yellowish needles, m. p. 215—216° (decomp.) (Found: N, 4·4; I, 36·3. $C_{10}H_6O_5NI$ requires N, 4·0; I, 36·6%). The same *product* was obtained by iodination of 5-hydroxy-2-methyl-6-nitrochromone [5] with iodine and iodic acid.

2 : 5-*Dihydroxy-3-iodo-4-methoxyacetophenone* (IVe).—The iodo-ketone (IVb) (1 g.) was dissolved in 10% aqueous sodium hydroxide (40 ml.) and oxidised with potassium persulphate (0·92 g. in 20 ml. of water) (cf. Baker and Brown [2]). The *product* crystallised from acetic acid in yellow needles (0·22 g.), m. p. 174° (decomp.) (Found: C, 35·0; H, 2·9; I, 41·1. $C_9H_9O_4I$ requires C, 35·0; H, 2·9; I, 41·2%).

2 : 5-*Dihydroxy-3-iodo-4-methoxybenzoic Acid* (Ve).—The iodo-acid (Vb) (1·5 g.) was oxidised as described before. The *product* crystallised from water in yellowish needles (0·3 g.), m. p. 212° (effervescence) (Found: C, 31·3; H, 2·5; I, 41·7. $C_8H_7O_5I$ requires C, 31·0; H, 2·3; I, 41·0%). The same product was obtained from the acid (Vc).

7-Hydroxy-6-iodo-2-methylchromone (IIId).—The di-iodo-chromone (IIIc) was refluxed with acetic acid for 4 hr. The solution became deep red. After cooling, it was added to ice-cold sodium hydrogen sulphite solution. The *product* crystallised in colourless needles (from acetic acid), m. p. 258—260° (decomp.) (Found: I, 42·5. $C_{10}H_7O_3I$ requires I, 42·1%). The *methyl ether* crystallised from alcohol in needles, m. p. 238° (Found: C, 41·4; H, 2·9; I, 40·7. $C_{11}H_9O_3I$ requires C, 41·8; H, 2·8; I, 40·2%).

One of us (M. V. S.) thanks the Government of India for a research scholarship.

ORGANIC CHEMISTRY LABORATORIES, MAHARAJA SAYAJIRAO UNIVERSITY OF BARODA, BARODA, INDIA. [*Received, January* 20*th*, 1959.]

[5] Naik and Thakor, *Proc. Ind. Acad. Sci.*, 1953, *A*, **37**, 774.

XUM

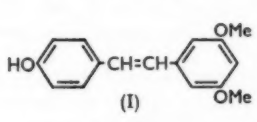
537. *West African Timbers. Part II.* Heartwood Constituents of the Genus* Pterocarpus.

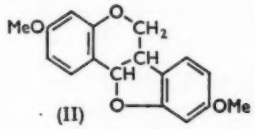
By A. Akisanya, C. W. L. Bevan, and J. Hirst.

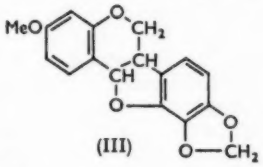
Four West African species, *Pterocarpus osun, P. erinaceous, P. mildbraedii, and P. santalinoides,* have been examined. Homopterocarpin, pterocarpin, angolensin, santal, and acetyloleanolic acid were isolated, but not pterostilbene. *P. santalinoides and P. mildbraedii,* which show very little resistance to decay, gave no phenolic compounds. The phytochemical significance of the results is discussed.

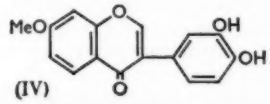
Erdtman,[1] in his work on the heartwood chemistry of the *Coniferales,* has shown that valuable taxonomic information may be so obtained. Thus, 3 : 5-dihydroxystilbene (pinosylvin) has been shown to be characteristic of more than 50 species of *Pinus,* and the subgenera *Haploxylon* and *Diploxylon* have also been characterised.

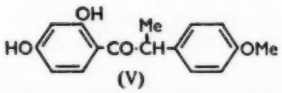
Less is known of the phylogenetic significance of heartwood chemistry in the dicotyledonous trees, the hardwoods of commerce. However, the discovery by King and his


(I)


(II)


(III)


(IV)


(V)

co-workers [2] of chlorophorin in *Chlorophora excelsa* [4] and of pterostilbene (I) in a number of species of *Pterocarpus* led them to suggest that stilbene derivatives may be characteristic of some genera. We have investigated four *Pterocarpus* species: *P. osun,* from which we obtained homopterocarpin (II), pterocarpin (III), acetyloleanolic acid, and santal (IV); *P. erinaceous,* yielding angolensin (V) and an unidentified substance, $C_{17}H_{14}O_6$; *P. santalinoides,* yielding arachidic acid and acetyloleanolic acid; and *P. mildbraedii,* from which also we obtained acetyloleanolic acid.

Heartwood extractives of Pterocarpus *species.*

	(I)	(III)	(II)	(V)	(A) *	(B) *	(C) *	(IV)
P. santalinus [a] ...	+	+	+					+
P. dalbergoides [b] ...	+	+						
P. macrocarpus [b] ...	+	+						
P. soyauxii [b]	+		+					
P. tinctorius [b]	+							
P. angolensis [b] ...				+	+	+	+	
P. osun		+	+		+			+
P. milbraedii					+			
P. erinaceous				+				
P. santalinoides ...					+	+		

* A = acetyloleanolic acid; B = arachidic acid; C = prunetin.

[a] Späth and Schläger, *Ber.,* 1940, **73**, 881. [b] Robertson, Suckling, and Whalley, *J.,* 1949, 1571.

The Table summarises the known constituents of *Pterocarpus* species. These species may be divided into four groups, with respect to resistance to decay. Five species contain pterostilbene, known to be strongly toxic to the brown rot fungus *Coniophora cerebella*; *P. angolensis* and *P. erinaceous* contain the phenolic ketone angolensin (V), while the very

* Part I, *W. African J. Biol. Chem.,* 1958, 36.

[1] Erdtman, "Perspectives in Organic Chemistry," Interscience Publ. Inc., New York, 1956, p. 453.

[2] King, Cotterill, Godson, Jurd, and King, *J.,* 1953, 3693.

XUM

similar *P. santalinus* and *P. osun* contain the isoflavone santal (IV), the non-phenolic pterocarpin and homopterocarpin, and two apparently similar red dyes.

It is remarkable that pterostilbene was not found in *P. osun*, although it was specially sought. Failure to identify it is no proof that it was not present, but it may be noted that while the probable biosynthetic route to pterostilbene (V) is *via* acetic acid [3] the other substances isolated are flavanoid and may arise from sugar molecules.

Finally, *P. mildbraedii* and *P. santalinoides* did not yield phenolic compounds, which is consistent with their lack of resistance to fungal and insect attack.

Experimental

Extractions were carried out under reflux in a copper apparatus. The powdered wood, on a wire gauze, was held in a cylindrical can open at both ends over the boiling solvent.

Constituents of Pterocarpus osun. (*a*) Powdered heartwood (3 kg.) was extracted with light petroleum (b. p. 60—80°) for 24 hr. Evaporation left a brown gum (30 g.) which gradually deposited white crystals. Fractional crystallisation from methanol gave homopterocarpin, m. p. and mixed m. p. 87—88°, $[\alpha]_D^{20}$ −207° (*c* 0·9 in $CHCl_3$) (Found: C, 71·5; H, 5·6; OMe, 20·5. Calc. for $C_{17}H_{16}O_4$: C, 71·8; H, 5·7; 2OMe, 21·8%), and the less soluble pterocarpin, m. p. and mixed m. p. 164·5°, $[\alpha]_D^{20}$ −212·8° (*c* 0·5 in $CHCl_3$) (Found: C, 68·5; H, 4·8; OMe, 10·3. Calc. for $C_{17}H_{14}O_5$: C, 68·5; H, 4·7; OMe, 10·4%). Both specimens were kindly provided by Professor F. E. King.

(*b*) The extract (15 g.) from powdered wood (1·5 kg.) was dissolved in ether (250 ml.) and extracted with N-sodium hydroxide (150 + 80 + 50 ml.). The alkaline extract was neutralised to pH 7 with acetic acid and extracted with ether, the extract washed and dried, and the ether removed. Crystallisation of the residue from methanol gave a trace of a solid, m. p. 78°, and acetyloleanolic acid, m. p. and mixed m. p. (with a specimen provided by Dr. T. G. Halsall) 257—259°.

(*c*) Powdered heartwood (8 kg.) was extracted for 12 hr. as before, and then for 12 hr. with ether. The ether extract was concentrated, and the residue refluxed with carbon tetrachloride (1 l.) for 6 hr. The carbon tetrachloride extract was evaporated under reduced pressure, and the residue, in ether (1 l.), extracted with potassium hydroxide solution (1 l. of 0·5%, then 5 × 1 l. of 5%). The extracts, acidified to pH 5, were extracted with ether (3 × 200 ml.). The ether extract was treated according to Späth and Schläger's method.[4] No pterostilbene was obtained, but after some months crystals separated. Sublimation at 225°/0·1 mm. gave santal, m. p. and mixed m. p. (with a specimen provided by Dr. W. B. Whalley) 222—223° (Found: C, 63·6; H, 3·8; OMe, 10·5. Calc. for $C_{15}H_{10}O_5$·OMe: C, 63·9; H, 4·0; OMe, 10·3%). Acetylation by the method of Robertson *et al.*[5] for ¼ hr. gave the acetate, m. p. 173—174° (Found: C, 62·0; H, 4·4; OAc, 28·0. Calc. for $C_{22}H_{18}O_9$: C, 62·0; H, 4·2; OAc, 30·0%). Acetylation for 24 hr. gave a compound, m. p. 144—146°, probably the diacetate noted by Robertson *et al.*[5]

Constituents of Pterocarpus erinaceous.—Powdered heartwood (3·8 kg.) was extracted as before for 12 hr. Evaporation gave a white solid (32 g.). This dissolved in ether but with a residue (0·7 g.) which on crystallisation from methanol–acetone gave a substance, m. p. 238—239° (decomp.) [Found: C, 65·9; H, 4·9; OMe, 10·0; *M* (Rast), 312. $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5; OMe, 9·5%; *M*, 327], $\lambda_{max.}$ 304 mμ (ε 11,860 in methanol). Its *acetate* had m. p. 152° (Found: OAc, 9·8. $C_{19}H_{16}O_7$ requires OAc, 11·6%).

The ether solution was washed with 2N-sodium hydroxide, and the alkali-soluble material crystallised from benzene–light petroleum (b. p. 60—80°) to give angolensin (10·8 g.), m. p. and mixed m. p. (with a specimen provided by Professor F. E. King) 121·5—122° (Found: C, 70·7; H, 5·7; OMe, 11·6. Calc. for $C_{16}H_{16}O_4$: C, 70·6; H, 5·9; OMe, 11·4%). With diazomethane it gave methylangolensin, m. p. 69° (Found: C, 71·5; H, 6·5; OMe, 21·8. Calc. for $C_{17}H_{18}O_4$: C, 71·3; H, 6·3; OMe, 21·7%).

Constituents of Pterocarpus santalinoides.—The powdered wood (10 kg.), extracted as before for 24 hr., gave an oil (40 g.) from which a white solid crystallised. Recrystallisation

[3] Robinson, "Structural Relations of Natural Products," Oxford University Press, 1957, p. 9.
[4] Späth and Schläger, *Ber.*, 1940, **73**, 881.
[5] Robertson, Suckling, and Whalley, *J.*, 1949, 1571.

XUM

from light petroleum gave a *substance*, m. p. 84° [Found: C, 75·6; H, 12·7%; *M* (Rast), 438. $C_{17}H_{35}\cdot CO_2H$ requires C, 76·0; H, 12·7%; *M*, 271]. Acids often give double molecular weights by the Rast method, but stearic acid has m. p. 69°. The residue, in ether, was washed with sodium hydroxide solution, and the acid fraction crystallised from methanol to give arachidic acid (0·6 g.), m. p. 78° [Found: C, 77·3; H, 12·5%; *M* (titration), 316. Calc. for $C_{20}H_{40}O_2$: C, 76·9; H, 12·9%; *M*, 312]. The *p*-bromophenacyl ester had m. p. 89°, and the methyl ester, m. p. 61°, in agreement with the literature. Concentration of the mother-liquor gave acetyloleanolic acid, m. p. 264—265°, $[\alpha]_D^{30}$ 70° (*c* 0·1 in $CHCl_3$) [Found: C, 77·3; H, 10·1; OAc, 7·0%; *M* (Rast), 454. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·1; OAc, 9·7%; *M*, 499]. Alkaline hydrolysis gave oleanolic acid, m. p. and mixed m. p. 303°.

Ingredients of Pterocarpus mildbraedii.—Powdered wood (10 kg.), extracted as before for 24 hr., gave an oil (30 g.). Acetyloleanolic acid was obtained as above, together with traces of two solids, m. p. 84° and 112°.

We are grateful to the Director of Forest Research, Ibadan, and to the Forestry Service, Nigeria, for gifts of timber and for its authentication and to Dr. T. G. Halsall for the spectra.

DEPARTMENT OF CHEMISTRY, UNIVERSITY COLLEGE,
IBADAN, NIGERIA. [*Received, February 20th*, 1959.]

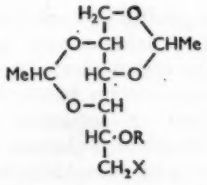
---

538. *Reaction of Some Alkyl Iodides with Periodate.*

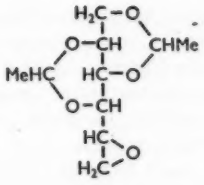
By A. B. FOSTER, M. STACEY, and R. W. STEPHENS.

Alkyl iodides are slowly attacked by periodate. Three mols. of oxidant are consumed in the ultimate conversion of the iodine into iodate ion with concomitant formation of hydrogen ions. Elemental iodine is an intermediate in the reaction. Alkyl chlorides and bromides are much less susceptible to attack although reaction is facilitated by vicinal carbonyl groups.

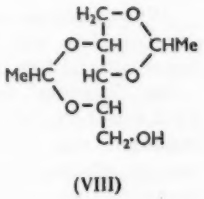
PERIODATE is known to cleave 1,2-glycols and related compounds.[1] However, other types of oxidation reaction have been recognized,[1,2] for example, the so-called over-oxidation [3] in which a methylene group is hydroxylated so that further cleavage becomes possible. Whilst studying α-halogenoacetaldehydes [4] we observed that alkyl iodides



(I), X = I, R = H. (II), X = Br, R = H.
(III), X = Cl, R = H. (IV), X = I, R = Ac.
(V), X = I, R = CO·Cl$_3$. (VI), X = OH, R = H.



(VII)



(VIII)

themselves are attacked by periodate. The reaction was first met with 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I) but may be general for alkyl iodides.

Reaction of 1,3-2,4-di-*O*-ethylidene-D-glucitol [5] (VI) with 1 mol. of toluene-*p*-sulphonyl

[1] See Bobbitt, *Adv. Carbohydrate Chem.*, 1956, **11**, 9.
[2] Greville and Northcote, *J.*, 1952, 1945.
[3] See, *e.g.*, Wolfrom and Bobbitt, *J. Amer. Chem. Soc.*, 1956, **78**, 2489.
[4] Bose, Foster, and Stephens, unpublished work.
[5] Appel, *J.*, 1935, 425; Bourne and Wiggins, *J.*, 1948, 1933.

XUM

chloride and then with acetic anhydride (both in pyridine) gave a 5-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl derivative which was converted [6] into 5,6-anhydro-1,3-2,4-di-*O*-ethylidene-D-glucitol (VII) by sodium methoxide. The same compound was less conveniently obtained by preparation of 1,3-2,4-di-*O*-ethylidene-6-*O*-toluene-*p*-sulphonyl-D-glucitol and its treatment with sodium methoxide.[7] The epoxide ring in compound (VII) was opened by methylmagnesium iodide,[6] to yield 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I). A better method of preparing the iodo-compound (I) involved treating the epoxide (VII) with hydriodic acid in aqueous tetrahydrofuran [8] at −10°. Under similar conditions the epoxide was converted into 6-bromo-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (II) by hydrobromic acid and into 6-chloro-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (III) by hydrochloric acid.

By comparison with the behaviour of similar compounds,[6,9] the epoxide derivative (VII) would be expected to yield 6-substituted products in these reactions. Attempts to prove this for the iodo-compound (I) by acidic hydrolysis of the ethylidene residues were unsuccessful. Under conditions (0·1N-sulphuric acid at 95° in an open vessel) where the ethylidene residues were removed from 1,3-2,4-di-*O*-ethylidene-D-glucitol (VI) in 3 hr. the alkyl iodide group in compound (I) was extensively, if not completely, hydrolysed. The iodo-compound (I) was reduced to 6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol by lithium aluminium hydride or by Raney nickel and hydrogen in the presence of sodium hydrogen carbonate; the deoxy-group in this compound is at position 6 because the deoxyhexitol produced by acidic hydrolysis reduces approximately 4 mol. of periodate. Similarly 6-bromo- and 6-chloro-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol each yielded a product on acidic hydrolysis which reduced approximately 4 mol. of periodate, confirming the 6-position of the halogen atoms. The alkyl chloride group of compound (III) remained intact during the acidic hydrolysis but the alkyl bromide group in the bromide (II) underwent *ca.* 11% of hydrolysis.

Acid-hydrolysis of alkylidene derivatives is usually performed in open vessels,[10] and, in the case of 1,3-2,4-di-*O*-ethylidene-D-glucitol, went smoothly to completion with no obvious break which would indicate a different rate of hydrolysis of the ethylidene residues. In sealed tubes, however, an equilibrium was rapidly established after the release of *ca.* 1·2 mol. of acetaldehyde, leaving a hexitol derivative (presumably [10] essentially 2,4-*O*-ethylidene-D-glucitol) which consumed 1·39 mol. of periodate. Work in sealed tubes may thus have some value for graded acid-hydrolysis of polyalkylidene carbohydrates.

When aqueous 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I) containing sodium metaperiodate was stored at room temperature, 4 mols. of oxidant were slowly consumed ($t_{\frac{1}{2}}$ *ca.*, 100 hr.; see Figure). Acid-hydrolysis of the carbohydrate product gave xylose (identified by chromatography), and reduction with sodium borohydride gave 1,3-2,4-di-*O*-ethylidene-D-xylitol identical with the product of sequential periodate oxidation and borohydride reduction of 1,3-2,4-di-*O*-ethylidene-D-glucitol (VI). (A racemic mixture would result from the reaction of xylitol with acetaldehyde.[10]) In a separate experiment, when 3·84 mol. of periodate had been consumed (after 593 hr.) by the 6-iodo-compound (I), 1·13 equiv. of hydrogen ion and 0·61 mol. of formaldehyde had been liberated. It is possible that, owing to the prolonged reaction and the presence of iodine, some oxidation of formaldehyde to formic acid occurred (cf. Davidson [11]). The reaction of the 6-iodo-compound (I) with periodate appeared not to be due to acid-hydrolysis of the alkyl iodide group (the pH of the periodate solutions used was 4·5) followed by oxidation of iodide ion. Thus iodide ion was not formed when aqueous solutions of the

[6] Cf. Foster and Overend, *J.*, 1951, 1132.
[7] Puskas and von Vargha, *Ber.*, 1943, **76**, 862.
[8] Cf. Lucas and Garner, *J. Amer. Chem. Soc.*, 1950, **72**, 2145.
[9] Wiggins and Wood, *J.*, 1950, 1566.
[10] See Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.
[11] Davidson, *J. Textile Inst.*, 1941, T117.

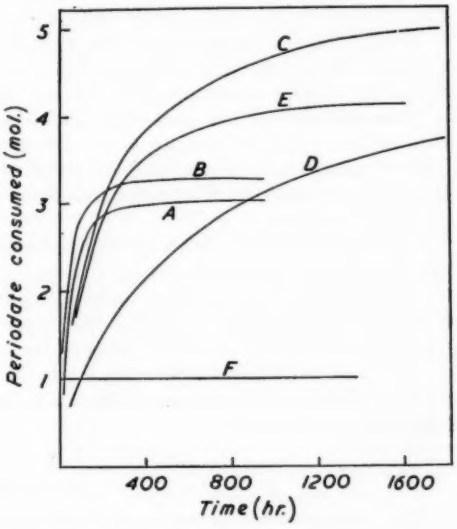
6-iodo-compound (I), acidified severally to pH 4·5 and 2·5, were stored for long periods. 1,3-2,4-Di-*O*-ethylidene-D-glucitol rapidly consumed 1 mol. of periodate at pH 4·5, but no further reaction occurred; the ethylidene residues were stable under these conditions.

These observations indicate the probable stoicheiometry of the reaction of 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I) with periodate as:

$$R{\cdot}CH(OH){\cdot}CH_2I + 4IO_4^- \longrightarrow R{\cdot}CHO + H{\cdot}CHO + 5IO_3^- + H^+ \quad . \quad . \quad . \quad . \quad (1)$$

$$I^- + 3IO_4^- \longrightarrow 4IO_3^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Mellor [12] records a complex reaction between periodate and iodide, but Willard and Greathouse [13] consider equation (2) to operate when excess of periodate and iodide react at 70—80°. Tolstikov [14] reports that the reaction proceeds in the pH range 4·3—7·0



Oxidation of alkyl iodides with periodate at room temperature. The solutions (100 ml.) contained approx. 0·68 mmole of alkyl iodide and 6·25 mmoles of sodium periodate. A, methyl iodide; B, ethyl iodide; C, iodoacetic acid; D, β-iodopropionic acid; E, 6-deoxy-1,3-2,4-di-O-ethylidene-6-iodo-D-glucitol; F, 1,3-2,4-di-O-ethylidene-D-glucitol.

and that iodate ions are amongst the products. Mixing aqueous solutions of sodium meta-periodate and sodium iodide caused rapid precipitation of iodine which then slowly disappeared; approximately three mols. of periodate were ultimately consumed with no change in pH of the medium. Willard and Greathouse's observations are thus confirmed. The 6-iodo-compound (I) (and each of the alkyl iodides studied) reacted with periodate, liberating iodine but to an extent never exceeding its solubility, so that the initial reaction of periodate with the alkyl iodide must be slow and essentially independent of subsequent reactions.

Methyl and ethyl iodide consume approximately 3 mol. of periodate (see Figure) with liberation of hydrogen ion. Iodoacetic acid reacted slowly (reaction incomplete after 2000 hr.) with the apparent consumption of 4 mol. of oxidant (see Figure) and liberation of formaldehyde and hydrogen ion. It seems probable that glycollic acid initially formed is itself slowly attacked by periodate. β-Iodopropionic acid consumed 5—6 mol. of periodate, liberating both hydrogen ion and formaldehyde. β-Hydroxypropionic acid,

[12] Mellor, " A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Longmans, London, 1922, Vol. II, p. 407.
[13] Willard and Greathouse, *J. Amer. Chem. Soc.*, **1938**, **60**, 2869.
[14] Tolstikov, *Sbornik Statei po obshchei Khim., Akad. Nauk S.S.S.R.*, **1953**, **2**, 1249; *Chem. Abs.*, 1955, **49**, 2921.

XUM

presumably an initial product of the reaction, is, surprisingly, slowly oxidised by periodate (0·25 mol. of oxidant consumed at pH 5·1 in 75 days at room temperature). This and related reactions will be discussed in detail in a separate paper.

The mechanism whereby alkyl iodides are attacked by periodate is not readily apparent. Conductivity measurements [15] indicate that alkyl halides are ionized to a limited extent so that, in the presence of periodate, oxidation to iodine and bromine would be expected and, since the ionization equilibria would be disturbed, would proceed to completion. Were this in fact the situation then any reagent capable of reacting rapidly with halide ions should also disturb the ionization equilibria and the rate of the reaction should be largely independent of the attacking species. This is not the case. Thus, with aqueous methyl iodide silver ions reacted completely within a few hours (cf. Gand [15,16] and Dostrovsky and Hughes [17]), periodate ions within a few days, iodate ions in presence of acid extremely slowly and cupric ions in neutral solution not detectably. It is possible that the reaction may proceed by the attack of periodate on the alkyl iodide in the form of an ion-pair.[18]

Under the conditions where the 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I) reacted with periodate the 6-bromo- and the 6-chloro-analogue were essentially unaffected. Similarly 1,2-dibromoethane was not attacked by periodate but ethyl bromoacetate, bromoacetaldehyde,[4] and chloroacetaldehyde [4] were. Although reaction of alkyl halides with periodate is slow compared with the usual rates of periodate oxidation, it should be borne in mind when the periodate oxidation of halogenated carbohydrates is contemplated. Moreover, a knowledge of the stoicheiometry of the reactions could be of value in certain structural studies.

Although 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol with acetic anhydride in pyridine readily gave a 5-acetate and with trichloroacetyl chloride a 5-trichloroacetate, toluene-*p*-sulphonylation could not be effected. Recovery of unchanged starting material from the last reactions suggested that there might be some steric hindrance but scale models revealed no obvious shielding of the hydroxyl group and apparently similar compounds give toluene-*p*-sulphonates.[19] It is of interest that Stork and White [20] have recorded that *trans*-6-alkyl-2-*cyclo*hexen-1-ols readily gave acetates but did not give toluene-*p*-sulphonates.

Experimental

The consumption of periodate was determined essentially by Jackson's method.[21]

6-Deoxy-6-halogeno-derivatives of 1,3-2,4-Di-O-ethylidene-D-glucitol.—(*a*) 5,6-Anhydro-1,3-2,4-di-*O*-ethylidene-D-glucitol [7,22] (0·43 g.) was added to boiling ethereal methylmagnesium iodide (3 ml.) [prepared from ether (275 ml.), magnesium (16·4 g.) and methyl iodide (93 g.)], and the mixture was boiled under reflux for 4 hr. After cooling to −10° the complex was decomposed with 2N-hydrochloric acid. To the separated ether layer were added two chloroform extracts of the aqueous layer, and the combined solutions were washed with aqueous sodium hydrogen carbonate (twice), then water (twice), dried ($MgSO_4$), and evaporated. Recrystallization of the residue (0·14 g., 20%) four times from benzene–light petroleum (b. p. 60—80°) gave 6-*deoxy*-1,3-2,4-*di*-O-*ethylidene*-6-*iodo*-D-*glucitol*, m. p. 151°, $[\alpha]_D^{21}$ −3·8° (*c* 4·5 in $CHCl_3$) (Found: C, 35·4; H, 5·1; I, 36·2. $C_{10}H_{17}O_5I$ requires C, 34·9; H, 5·0; I, 36·9%). The poor yield is probably due to the low solubility of the anhydro-compound in ether.

(*b*) A stirred solution of 5,6-anhydro-1,3-2,4-di-*O*-ethylidene-D-glucitol (6 g.) in tetrahydrofuran (100 ml.) at −15° was treated with 56% hydriodic acid (3·88 ml., 1·04 mol.), so that the temperature did not rise above 0°. The solution was then stored at −5°, and the consumption

[15] Gand, *Ann. Fac. sci. Marseille*, 1939, **12**, 134; *Chem. Abs.*, 1941, **35**, 681.
[16] Gand, *Bull. Soc. chim. France*, 1945, **12**, 303.
[17] Dostrovsky and Hughes, *J.*, 1946, 169.
[18] Winstein, 14th Congr., Internat. Union Pure Appl. Chem., *Experientia*, 1957, Suppl. 2, p. 149.
[19] Foster and Overend, *J.*, 1951, 3452.
[20] Stork and White, *J. Amer. Chem. Soc.*, 1956, **78**, 4609.
[21] Jackson, "Organic Reactions," 1944, Vol. II, p. 361.
[22] Wiggins, *J.*, 1946, 388.

of acid followed by titration of aliquot parts with standard sodium hydroxide solution; reaction was essentially complete in 10 hr. After 43 hr. sodium thiosulphate and potassium carbonate were added to remove free iodine and excess of acid, followed by sufficient water to form two phases. The organic layer was separated and evaporated and the residue extracted several times with chloroform. The combined extracts were dried ($MgSO_4$) and concentrated to yield a residue (8·13 g., 86%) having m. p. 145—146° which was not changed by recrystallization from benzene–light petroleum (b. p. 60—80°). The yields of 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol in a series of experiments were in the range 45—86% and the m. p.s of various preparations, although sharp in each case, varied within the range 144—153°.

By essentially the same procedure, 5,6-anhydro-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·2 g.) in tetrahydrofuran (12 ml.) with 45·5% hydrobromic acid (0·123 ml., 1·1 mol.) gave 6-*bromo*-6-*deoxy*-1,3-2,4-*di*-O-*ethylidene*-D-*glucitol* (0·27 g., 98%) which after recrystallization from benzene–light petroleum (b. p. 60—80°) had m. p. 141—143°, $[\alpha]_D^{21}$ −4·1° (*c* 4·4 in $CHCl_3$) (Found: C, 40·1; H, 5·7; Br, 26·3. $C_{10}H_{17}O_5Br$ requires C, 40·4; H, 5·8; Br, 26·9%).

Treatment of a solution of the anhydro-compound (0·2 g.) in tetrahydrofuran (10 ml.) with 10·4N-hydrochloric acid (0·107 ml., 1·2 mol.) essentially as above gave 6-*chloro*-6-*deoxy*-1,3-2,4-*di*-O-*ethylidene*-D-*glucitol* (0·08 g., 38%, after recrystallization from benzene–light petroleum), m. p. 156—158°, $[\alpha]_D^{21}$ +0·3° (*c* 3·3 in $CHCl_3$) (Found: C, 47·7; H, 6·7; Cl, 14·0. $C_{10}H_{17}O_5Cl$ requires C, 47·5; H, 6·8; Cl, 14·0%). Yields of *ca.* 70% were obtained in subsequent preparations.

The halogeno-compounds were all soluble in water, and in certain of the preparations, irrespective of the halogen being introduced, a small amount of a water-insoluble, halogen-free compound was obtained, which, after recrystallization from ethanol, had m. p. 168—169° (Found: C, 53·25; H, 5·8%); the molecular weight (Rast in camphor [23]) (455 ± 60) suggested some type of dimerization.

6-Deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol with acetic anhydride and pyridine gave a 5-*acetate*, m. p. 128—129°, $[\alpha]_D^{21}$ −35·7° (*c* 4·4 in $CHCl_3$) (Found: C, 37·5; H, 5·0; I, 32·6. $C_{12}H_{19}O_6I$ requires C, 37·3; H, 5·0; I, 32·9%), and with trichloroacetyl chloride in pyridine gave a 5-*trichloroacetate*, m. p. 130·5—131·5°, $[\alpha]_D^{21}$ −38·3° (*c* 6·1 in $CHCl_3$) (Found: C, 29·3; H, 3·1; I, 25·7. $C_{12}H_{16}O_6Cl_3I$ requires C, 29·4; H, 3·3; I, 25·9%).

Acid-hydrolysis of 1,3-2,4-*Di*-O-*ethylidene*-D-*glucitol*.—(a) *In a sealed tube.* 1,3-2,4-Di-*O*-ethylidene-D-glucitol (2 g.) was dissolved in a small volume of water, 5N-sulphuric acid (10 ml.) was added, and the volume adjusted to 50 ml. Aliquot parts (4 ml.) were sealed in ampoules and immersed in boiling water. At suitable intervals ampoules were cooled to −10°, and a portion (1 ml.) of the contents diluted with water to 10 ml. Vicinal glycol groups were determined by periodate oxidation, and acetaldehyde essentially by Dyer's method.[24] Equilibrium was established in <10 min., 1·2 mol. of acetaldehyde being liberated, and the remaining carbohydrate consumed 1·39 mol. of periodate.

(b) *In an open vessel.* Hydrolyses at 95° involved (1) a 0·16% solution of 1,3-2,4-di-*O*-ethylidene-D-glucitol in N-sulphuric acid and (2) a 5·3% solution in 0·1N-sulphuric acid, with the following results:

(1)	Time (min.)	0	5	10	15		
	IO_4 consumption (mol.)	1·04	4·42	4·99	5·05		
(2)	Time (min.)	0	22	44	50	120	160
	IO_4 consumption (mol.)	1·10*	2·42	3·42	4·00	4·65	4·92

* This portion stored at room temperature for 3·5 hr. before analysis.

Reduction of 6-*Deoxy*-1,3-2,4-*di*-O-*ethylidene*-6-*iodo*-D-*glucitol*.—(*a*) To a solution of lithium aluminium hydride (0·83 g., 4 mol.) in dry ether (20 ml.), 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (2 g.) was added and the mixture boiled for 6·5 hr. Excess of hydride was destroyed with ethyl acetate, water was added, and the aqueous solution was extracted with ethyl acetate and then chloroform. The combined extracts were evaporated, the residue was extracted with chloroform and the dried ($MgSO_4$) extracts were evaporated. Recrystallization

[23] Linstead, Elvidge, and Whalley, "Modern Techniques of Organic Chemistry," Butterworths, London, 1955, p. 145.
[24] Dyer, "Methods of Biochemical Analysis," Interscience, New York, 1956, Vol. III, p. 129.

XUM

of the residue (0·56 g., 44%) from ethanol–light petroleum (b. p. 60—80°) gave *6-deoxy-1,3-2,4-di-O-ethylidene-D-glucitol*, m. p. 178—179°, $[\alpha]_D^{21}$ −8·9° (*c* 1·5 in $CHCl_3$) (Found: C, 55·4; H, 8·4. $C_{10}H_{18}O_5$ requires C, 55·1; H, 8·3%).

(*b*) Raney nickel (*ca.* 0·1 g.; W-2), platinum oxide (*ca.* 10 mg.), and saturated aqueous sodium hydrogen carbonate (4 ml.) were added to a solution of 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (1 g.) in ethanol (6 ml.). The mixture was shaken in hydrogen at a slight overpressure; hydrogen consumption (70 ml., 1 mol.) was complete within 3 hr. The filtered solution was evaporated and the residue extracted several times with ethyl acetate. Evaporation of the extracts and recrystallization of the residue from ethanol–light petroleum (b. p. 60—80°) gave 6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·2 g., 41%), m. p. 173—174°.

Acid-hydrolysis and Periodate Oxidation of 6-Deoxy-1,3-2,4-di-O-ethylidene-D-glucitol and its 6-Bromo- and 6-Chloro-derivatives.—6-Bromo-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·1017 g., 0·342 mmole), 6-chloro-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·08645 g., 0·342 mmole), and 6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·0746 g., 0·342 mmole) were severally dissolved in 0·2N-sulphuric acid (5 ml.), and the solutions heated at 95° for 3 hr. The consumptions of periodate were: 6-bromo-6-deoxy-compound 3·96 mol.; 6-chloro-6-deoxy-compound 3·97 mol.; 6-deoxy-compound 4·12 mol. The value for the bromo-compound is corrected for a small amount (11·3%) of hydrolysis of the alkyl bromide.

Action of Periodate on 6-Deoxy-1,3-2,4-di-O-ethylidene-6-iodo-D-glucitol.—(*a*) To a solution of the iodo-compound (0·2352 g., 0·684 mmole) in water was added 0·25M-sodium metaperiodate (25 ml., 8·8 mmoles), and the volume adjusted to 100 ml. A similar solution containing 1,3-2,4-di-*O*-ethylidene-D-glucitol (0·16 g., 0·684 mmole) was prepared for comparison. The solutions were stored at room temperature in the dark and the following consumption of periodate observed:

Time (hr.)	25	48	93	144	281	619	955	1296
IO_4 consumption (mol.) ...	0·62	1·17	1·70	2·38	3·20	3·83	4·03	4·13

After 2·5 hr. 1,3-2,4-di-*O*-ethylidene-D-glucitol had consumed 1·02 mol. of periodate; no further uptake occurred during the next 1000 hr.

During the oxidation of the iodo-compound, free iodine was produced although its concentration never exceeded its solubility and it had disappeared after 950 hr. This was observed in all oxidations of the iodides in aqueous solution by sodium metaperiodate.

After 355 hr. an aliquot part (5 ml.) of the reaction solution containing the iodo-compound was treated with ethylene glycol (1 ml.) for 5 min., then 0·5N-sulphuric acid (2 ml.) was added and the solution boiled for 3 hr. The hydrolysate was neutralized with barium carbonate, then filtered, and the filtrate concentrated to small bulk. Analysis of the concentrate by paper chromatography on Whatman No. 4 paper with a formic acid–acetic acid–water–ethyl acetate (1 : 3 : 4 : 8) solvent system and detection with aniline hydrogen phthalate [25] revealed a single reducing component with properties identical with those of D-xylose.

(*b*) An aqueous solution of sodium metaperiodate and 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol identical with that described in (*a*) was stored in the dark at room temperature. The consumption of periodate was followed, as were the liberation of hydrogen ion (by Dyer's method [24]) and the production of formaldehyde (by the chromotropic acid method [26]). After 593 hr. 3·84 mol. of periodate had been consumed ($t_{\frac{1}{2}}$ oxidation 140 hr.), 1·13 equiv. of H^+ and 0·61 mol. of formaldehyde being liberated. Reaction was still proceeding after 2000 hr. The pH values of solutions of the iodo-compound (50 mg.) in water (25 ml.) were adjusted to 4·5 and 2·5 by dilute sulphuric acid, and the mixtures were stored at room temperature. Iodide ions were not released during 750 hr.

1,3-2,4-Di-O-ethylidene-D-xylitol.—(*a*) A solution of 1,3-2,4-di-*O*-ethylidene-D-glucitol (3 g.) and sodium metaperiodate (5·37 g., 2 mol.) in water (60 ml.) was stored at room temperature for 20 min. and then continuously extracted with benzene for 20 hr. Evaporation of the extract gave a syrupy residue (1·83 g.) which was dissolved in water (20 ml.) and treated with sodium borohydride (0·52 g.) for 5 hr. at room temperature. Excess of hydride was decomposed with dilute acetic acid, and the solution basified with sodium hydrogen carbonate and continuously extracted with benzene for 20 hr. Evaporation of the extract and recrystallization

[25] Partridge, *Nature*, 1949, **164**, 443.
[26] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.

of the residue (1·5 g.) from ethanol gave 1,3-2,4-*di*-O-*ethylidene*-D-*xylitol*, m. p. 161—162°, $[\alpha]_D^{21}$ +5·6° (*c* 4·5 in $CHCl_3$) (Found: C, 52·8; H, 7·9. $C_9H_{16}O_5$ requires C, 52·9; H, 7·9%).

(*b*) An aqueous solution (1 l.) containing 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (2·352 g.) and sodium metaperiodate (13·35 g.) was stored at room temperature for 29 days. Reaction was then complete. 200 ml. of the solution were continuously extracted with benzene for 4 days. Concentration of the extract gave a syrupy residue (0·276 g.) which on reduction with sodium borohydride as described in (*a*) gave 1,3-2,4-di-*O*-ethylidene-D-xylitol, m. p. and mixed m. p. 154—156°.

Comparison of Reaction of Sodium Metaperiodate with the 6-Iodo-, 6-Bromo-, and 6-Chloro-derivatives of 6-Deoxy-1,3-2,4-di-O-ethylidene-D-glucitol.—Aqueous solutions (100 ml.) containing 0·684 mmole of halogeno-derivative and sodium metaperiodate (equivalent to 25 ml. of a 0·25M-solution) were stored at 25—26° in the dark. The consumptions of periodate were:

Time (hr.)		20	63	119	164	239	354
IO_4 reduced (mol.) :	iodide	1·1	2·21	3·14	3·55	3·94	4·25
	bromide	—	—	0·04	—	—	0·05
	chloride	—	—	0·05	—	—	0·06

Action of Sodium Metaperiodate on Sodium Iodide.—To a solution of sodium iodide (0·051 g., 0·342 mmole) in water, 0·25M-sodium metaperiodate (11 ml.) was added and the volume adjusted to 50 ml. Iodine was immediately precipitated. After 7 days the mixture was free from insoluble iodine and the consumption of periodate was followed thereafter:

Time (days)	7	8	10	12
Consumption (mol.)	2·84	2·87	2·92	2·93

The pH of the mixture was initially and finally 4·4.

Action of Sodium Metaperiodate on Some Alkyl Halides.—Solutions of methyl iodide (0·1008 g., 0·710 mmole), ethyl iodide (0·1022 g., 0·655 mmole), iodoacetic acid (0·1275 g., 0·684 mmole), and β-iodopropionic acid (0·1371 g., 0·684 mmole) severally in water (100 ml.) containing sodium metaperiodate (equivalent to 25 ml. of 0·25M-solution) were stored at room temperature in the dark. The consumption of periodate was followed, with the results shown in the Figure. The hydrogen ion and formaldehyde production were determined by the methods previously noted and the following results were obtained:

	H^+ (equiv.) after 1048 hr.	CH_2O (mol.) after 1390 hr.	CH_2O (mol.) after 2611 hr.
MeI	0·73	—	—
EtI	0·71	—	—
$CH_2I{\cdot}CO_2H$	1·16	0·35	0·48
$CH_2I{\cdot}CH_2{\cdot}CO_2H$	1·5	0·52	0·65

Under similar conditions 1,2-dibromoethane did not react with periodate but ethyl bromoacetate reacted slowly with the formation of bromine.

Reaction of Methyl Iodide with Ag^+, Cu^{++}, *and* IO_3^-.—To a saturated (0·082M) aqueous solution (50 ml.) of methyl iodide the following aqueous solutions were severally added: 0·95N-silver nitrate (25 ml.), N-copper sulphate (25 ml.), and N-potassium iodate (25 ml.). No reaction of methyl iodide was apparent in the presence of Cu^{++} after several weeks; an immediate slight colour was formed in the iodate solution and slowly intensified as iodine was released; there was an immediate precipitate of silver iodide [4] in the presence of Ag^+, essentially complete within 2 hr.

CHEMISTRY DEPARTMENT, UNIVERSITY OF BIRMINGHAM. [*Received, February 23rd,* 1959.]

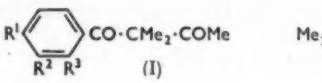
XUM

539. *The Rearrangement of Non-enolisable β-Diketones. Part I.**

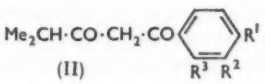
By N. H. Bromham and A. R. Pinder.

Some further examples of the rearrangement of non-enolisable β-diketones (I) are described. The transformations are promoted by sodium suspended in purified ether, which seems to exclude an intermolecular mechanism of fission and re-synthesis; the diketone (I; $R^2 = NO_2$, $R^1 = R^3 = H$) is stable to sodium in ether, which suggests that the change is not analogous to the intramolecular Baker–Venkataraman rearrangement. Two related cases involving the migration of an acetyl group are described.

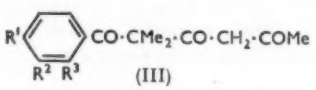
During experiments on steroid synthesis [1] it was observed that the non-enolisable β-diketone, α-acetylisobutyrophenone (I; $R^1 = R^2 = R^3 = H$) was transformed by sodium in ether containing a trace of ethanol into α-isobutyrylacetophenone (II; $R^1 = R^2 = R^3 = H$). It was of interest to explore the scope of this rearrangement, and to attempt to elucidate its mechanism.



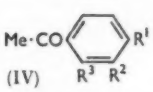
(I)



(II)



(III)



(IV)

Several diketones of the general formula (I) have therefore been prepared, chiefly by the acetylation of the corresponding isobutyrophenones with acetic anhydride and boron trifluoride.[2] The diketones were always accompanied by small yields of the triketones [3] (III), from which they were easily separated because of the solubility of the latter in alkali. The diketone (I; $R^1 = OMe$, $R^2 = R^3 = H$) was not obtainable by this method of acylation, owing to the deactivating influence of the 4-methoxyl group on the methinyl hydrogen atom in 4-methoxyisobutyrophenone. It was, however, formed when the latter was converted into its sodium enolate, and then treated with acetyl chloride.[4]

The diketones, which gave no colour with ferric chloride and showed two distinct carbonyl bands in their infrared spectra, were mixed in dry ethereal solution with a suspension of powdered sodium in dry ether. Usually, a vigorous reaction set in after a few minutes, and cooling had to be applied. In the original work [1] ethyl acetate was present or a trace of ethanol was added, but it has now been found that the reactions proceed without special addition of these substances; this has been confirmed by other workers [5] for the diketone (I; $R^1 = R^2 = R^3 = H$). The products were isolated by decomposition with ice, alkaline extraction, acidification, and ether-extraction, substituted benzoic acids, which were usually formed simultaneously, being removed by washing with sodium hydrogen carbonate. The products were characterised as their copper complexes. Authentic specimens of the expected rearrangement products were synthesised by Claisen-type condensations between the appropriate acetophenone (IV) and ethyl isobutyrate.[6]

Of the diketones studied, α-acetyl-4-methyl- and -4-chloro-isobutyrophenone (I; $R^1 =$ Me or Cl, $R^2 = R^3 = H$) rearranged to give the corresponding enolic diketones (II), though

* For a preliminary report see *Chem. and Ind.*, 1959, 258.

[1] Pinder and Robinson, *J.*, 1955, 3341.

[2] Hauser, Swamer, and Adams, in "Organic Reactions," Wiley, New York, 1954, Vol. VIII, pp. 129 *et seq.*

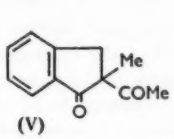
[3] Cf. ref. 1 and Walker, Sanderson, and Hauser, *J. Amer. Chem. Soc.*, 1953, **75**, 4109.

[4] Cf. Hudson and Hauser, *ibid.*, 1941, **63**, 3156, 3163.

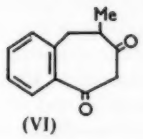
[5] Inamoto, Iwata, and Simamura, *Chem. and Ind.*, 1959, 47.

[6] Ref. 2, Chapter 3.

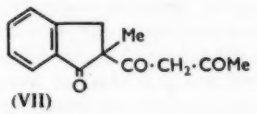
the yield in the latter case was very poor. α-Acetyl-4-methoxyisobutyrophenone (I; R^1 = OMe, $R^2 = R^3 = H$) reacted vigorously with sodium, to give a product showing enolic properties, but its copper complex could not be obtained crystalline; it was, however, concluded that the product contained some of the expected enolic diketone (II) because on



(V)



(VI)



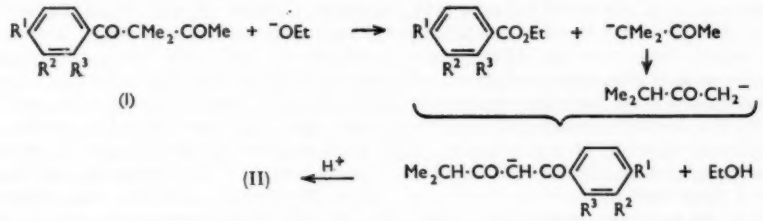
(VII)

$Me{\cdot}CO{\cdot}CMe_2{\cdot}COMe$ (VIII)

$Me_2CH{\cdot}CO{\cdot}CH_2{\cdot}COMe$ (IX)

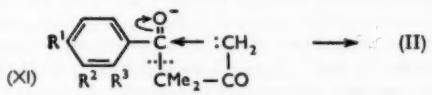
$Ph{\cdot}CO{\cdot}C(=CHPh){\cdot}COMe$ (X)

treatment with Brady's reagent in alcoholic sulphuric acid it afforded 4-methoxyacetophenone 2,4-dinitrophenylhydrazone. α-Acetyl-2,4-dimethylisobutyrophenone (I; $R^1 = R^3 = Me$, $R^2 = H$) also reacted energetically with sodium, giving a poor yield of an enolic product, from which a crystalline copper complex could not be derived; an infrared comparison between the product and α-isobutyryl-2,4-dimethylacetophenone (II; $R^1 = R^3 = Me$, $R^2 = H$) was complicated by the fact that the former contained 2,4-dimethylbenzoic acid, even after repeated washing with sodium hydrogen carbonate.



On the other hand α-acetyl-3-nitroisobutyrophenone (I; $R^1 = R^3 = H$, $R^2 = NO_2$) proved to be stable to sodium under these conditions, and was recovered unchanged.

The reaction of 2-acetyl-2-methylindan-1-one (V) with sodium afforded, not the expected benzocycloheptanedione (VI), but 2-acetoacetyl-2-methylindan-1-one (VII), the formation of which involves the separation of an acetyl group, followed by attack on another molecule of starting material. A case involving the migration of an acetyl group is provided by the isomerisation of 3,3-dimethylacetylacetone (VIII) to isobutyrylacetone (IX). 3-Benzylidenebenzoylacetone (X) did not react with sodium.



Two mechanisms have been suggested briefly for the rearrangements.[1] In the first, an intermolecular change has been postulated in which fission of an acyl group, under the influence of an ethoxide anion, affords an ester. This then condenses with the terminal reactive methyl group, with the formation of the new β-diketone and regeneration of ethanol. Only a catalytic quantity of sodium ethoxide would therefore be required, the transformation of (I) into (II) being as illustrated. This mechanism must be excluded, apparently, because the rearrangement is promoted by sodium alone, in the absence of ethanol, this view being strengthened by recent tracer studies on the rearrangement of the diketone (I; $R^1 = R^2 = R^3 = H$).[5]

A second possible mechanism is based on an analogy with the Baker–Venkataraman

rearrangement of *o*-aroyloxyacetoarones,[7] which has been shown by Wheeler *et al.*[8] to be intramolecular. By analogy, the rearrangement of the diketone (I) would involve a transition state (XI), and would be expected to be facilitated by the presence of strongly electron-attracting groups in the migrating nucleus, as is the case with the Baker–Venkataraman change.[8b] The failure of the nitro-diketone (I; $R^1 = R^3 = H$, $R^2 = NO_2$) to rearrange, however, suggests that this mechanism is not operative, and further experiments are now being carried out in an effort to elucidate this aspect of the rearrangement.

The behaviour of 2-acetyl-2-methylindan-1-one (V) indicates that, in this case at least, an acetyl group is cleaved from the molecule, and if it can be assumed that the true isomerisations occur by a similar process, the mechanism involved must be intermolecular.

As far as we are aware, these transformations represent the first recorded cases of the migration of an acyl group from one carbon atom to another in the same molecule, apart from a rearrangement involving the migration of an ethoxycarbonyl group in a Michael reaction.[9]

Experimental

α-Acetyl-4-methylisobutyrophenone.—4-Methylisobutyrophenone [10] (88 g.) in acetic anhydride (204 g., 2 mol.) was saturated with boron trifluoride at 0° during 2 hr., with stirring. The syrupy product was poured on ice-cold, concentrated sodium acetate solution, and the oil liberated was isolated with ether, washed several times with cold 4% aqueous sodium hydroxide, then with water, dried (Na_2SO_4), and recovered; fractionation gave *α-acetyl-4-methylisobutyrophenone*, b. p. 109—110°/1·2 mm. (21%) (Found: C, 76·9; H, 8·2. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%), with a fore-run of unchanged monoketone and some residue. Infrared C=O bands (liquid film) were at 1670 (phenyl conjugated) and 1743 cm.$^{-1}$ (unconjugated). Hydrolysis with boiling dilute sulphuric acid afforded acetic acid (*S*-benzylthiuronium salt, m. p. and mixed m. p. 136°) and 4-methylisobutyrophenone (semicarbazone, m. p. and mixed m. p. 101°). A *monosemicarbazone* crystallised from 50% aqueous ethanol in needles, m. p. 196·5° (Found: C, 64·3; H, 7·4; N, 15·9. $C_{14}H_{19}O_2N_3$ requires C, 64·4; H, 7·3; N, 16·1%).

Reaction of α-Acetyl-4-methylisobutyrophenone with Sodium.—The following conditions are typical of those used in these investigations. Ether (Macfarlan's; distilled over sodium) was kept for 7—10 days over fresh sodium wire. In carefully dried apparatus the above diketone (5·0 g.) in dry ether (15 c.c.) was added dropwise to a suspension of powdered sodium (1·1 g.; 2 g.-atoms; weighed under dry light petroleum and powdered in dry xylene), with swirling, precautions being taken to exclude moisture. A reaction developed gradually; after a few minutes it had become quite vigorous and gentle cooling was applied. After 24 hr. most of the sodium had dissolved and the mixture was cooled and decomposed with ice. The ether layer was separated and washed with a little water, and the combined aqueous layers were acidified with 5N-hydrochloric acid, with cooling. The oil liberated was taken up in ether, washed with sodium hydrogen carbonate solution and water, dried, and recovered. The residual *α-isobutyryl-4-methylacetophenone* (*4-methyl-1-p-tolylpentane-1,3-dione*) (II; $R^1 = Me$, $R^2 = R^3 = H$) distilled at 130—138° (bath)/0·2 mm. (0·3 g.) (Found: C, 76·6; H, 7·6. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%), was soluble in dilute aqueous sodium hydroxide, and gave a wine-red ferric colour. The *copper complex* crystallised from light petroleum in pale blue rhombic prisms, m. p. 187° (Found: C, 66·4; H, 6·9. $C_{26}H_{30}O_4Cu$ requires C, 66·4; H, 6·4%). With 2,4-dinitrophenylhydrazine the product afforded *1-(2,4-dinitrophenyl)-3(or 5)-isopropyl-5(or 3)-p-tolylpyrazole*, orange plates (from ethanol), m. p. 154° (Found: C, 61·9; H, 5·1; N, 15·3. $C_{19}H_{18}O_4N_4$ requires C, 62·3; H, 4·9; N, 15·3%). Acidification of the sodium hydrogen carbonate washings gave *p*-toluic acid, m. p. and mixed m. p. 177°.

α-Isobutyryl-4-methylacetophenone.—4-Methylacetophenone [11] (13·4 g.) in dry ether (100 c.c.) was added dropwise, with swirling, to an ethereal 0·15M-, solution of sodium triphenylmethyl

[7] Baker, *J.*, 1933, 1381; 1934, 1953; Mahal and Venkataraman, *Current Sci.*, 1933, **2**, 214; *J.*, 1934, 1767; Bhalla, Mahal, and Venkataraman, *J.*, 1935, 868.

[8] (*a*) Wheeler, *Chem. and Ind.*, 1947, 753, and references there cited; (*b*) Doyle, Gogan, Keane, and Wheeler, *Proc. Roy. Dublin Soc.*, 1948, **24**, 291.

[9] Simamura, Inamoto, and Suehiro, *Bull. Chem. Soc. Japan*, 1954, **27**, 221.

[10] Claus, *J. prakt. Chem.*, 1892, **46**, 480.

[11] Noller and Adams, *J. Amer. Chem. Soc.*, 1924, **46**, 1889.

(733 c.c.; 1·1 mol.), followed by ethyl isobutyrate (11·6 g., 1 mol.) in dry ether (100 c.c.), the whole operation being conducted in dry nitrogen. After 12 hr., with occasional agitation, water was added and the aqueous layer separated, cooled, and acidified. α-Isobutyryl-4-methylacetophenone distilled at 155—156°/10 mm. (4·0 g.) (Found: C, 76·5; H, 8·0%). The copper complex, and the pyrazole formed with 2,4-dinitrophenylhydrazine, had respectively m. p. 187° and 154°, undepressed by admixture with the derivatives described in the previous paragraph. Acid-hydrolysis afforded 4-methylacetophenone 2,4-dinitrophenylhydrazone (m. p. and mixed m. p. 250°).

α-Acetyl-2,4-dimethylisobutyrophenone (I; $R^1 = R^3 = Me$, $R^2 = H$).—Acetylation of 2,4-dimethylisobutyrophenone [12] (14·9 g.) with acetic anhydride (17·4 g.) and boron trifluoride, as described above, gave, after distillation through a 15 cm. Vigreux column, *α-acetyl-2,4-dimethylisobutyrophenone*, b. p. 105—108°/0·3 mm., 96—100°/0·05 mm. (3·1 g.) (Found: C, 76·4; H, 8·3. $C_{14}H_{18}O_2$ requires C, 77·0; H, 8·3%), with unchanged ketone and residual tar. Infrared C=O bands (liquid film) were at 1674 (phenyl conjugated) and 1743 cm.$^{-1}$ (unconjugated).

When an ethereal solution of the diketone was mixed with a suspension of powdered sodium in ether a vigorous reaction occurred within a few minutes. Working up as above gave 2,4-dimethylbenzoic acid (m. p. and mixed m. p. 126—127°) with a trace of a yellow liquid, b. p. about 128° (bath)/0·05 mm., which gave a deep red colour with ferric chloride. It also formed a copper complex (green solution in ether), but this could not be obtained crystalline. A direct infrared comparison with authentic α-isobutyryl-2,4-dimethylacetophenone (see below) indicated that the two were not identical, but the comparison was complicated by the difficulty of removing all the 2,4-dimethylbenzoic acid from the product.

α-Isobutyryl-2,4-dimethylacetophenone [13] [*4-methyl-1-(2,4-xylyl)pentane-1,3-dione*] (II; $R^1 = R^3 = Me$, $R^2 = H$).—Alcohol-free sodium ethoxide, from sodium (4·6 g.), was suspended in dry ether (50 c.c.), containing ethyl isobutyrate (23·2 g.). 2,4-Dimethylacetophenone [14] (14·8 g.) in dry ether (50 c.c.) was added, with shaking, and the mixture kept at room temperature for 48 hr. After decomposition with ice, the aqueous layer was separated, acidified, and extracted with ether. The extract, after being washed several times with sodium hydrogen carbonate, was dried and concentrated. The *diketone* distilled at 110—115° (bath)/0·05 mm. and had m. p. *ca.* 25° (2·4 g.) (Found: C, 77·4; H, 8·1. $C_{14}H_{18}O_2$ requires C, 77·1; H, 8·3%). The *copper complex* crystallised from ether–light petroleum (b. p. 40—60°) in dark green elongated prisms, m. p. 158—159°.

α-Acetyl-4-chloroisobutyrophenone (I; $R^1 = Cl$, $R^2 = R^3 = H$).—4-Chloroisobutyrophenone was obtained by Friedel–Crafts acylation of chlorobenzene; [15] it had b. p. 141—142°/17—18 mm., which differs from a recorded value [15] (122—123°/25 mm.), but is in agreement with that given by Bayless and Hauser,[16] who obtained the ketone by a different method. The infrared C=O band (liquid film) was at 1680 cm.$^{-1}$. The *2,4-dinitrophenylhydrazone* separated from ethanol in orange-yellow plates, m. p. 139·5—140° (Found: C, 53·0; H, 4·5. $C_{16}H_{15}O_4N_4Cl$ requires C, 53·0; H, 4·2%). The ketone (9·8 g.), dissolved in acetic anhydride (13·4 g.), was saturated with boron trifluoride at 0° during 1½ hr. Working up in the usual manner gave, after removal of the alkali-soluble material and fractional distillation *via* a 15 cm. Vigreux column, *α-acetyl-4-chloroisobutyrophenone*, b. p. 115—116°/0·3 mm. (4·7 g.) (Found: C, 63·8; H, 6·0. $C_{12}H_{13}O_2Cl$ requires C, 64·2; H, 5·8%), $\nu_{max.}$ (liquid film) 1670 (C=O conjugated with benzene ring) and 1738 cm.$^{-1}$ (unconjugated). A *monosemicarbazone* separated from aqueous methanol in irregular prisms, m. p. 185·5° (Found: C, 55·3; H, 5·2. $C_{13}H_{16}O_2N_3Cl$ requires C, 55·4; H, 5·7%). Acidification of the alkaline washings obtained in the working-up of the diketone afforded *1-p-chlorophenyl-2,2-dimethylhexane-1,3,5-trione* (III; $R^1 = Cl$, $R^2 = R^3 = H$), isolated with ether. It distilled at 135° (bath)/0·25 mm. (0·7 g.) (Found: C, 63·3; H, 5·5. $C_{14}H_{15}O_3Cl$ requires C, 63·0; H, 5·6%) and gave a conjugate chelate spectrum (liquid film), with a non-enolisable carbonyl band at 1669 cm.$^{-1}$. The *copper complex* crystallised from benzene–light petroleum (b. p. 60—80°; 1 : 2) in bluish-grey rhombic prisms, m. p. 201° (decomp.) (Found: C, 56·5; H, 4·4. $C_{28}H_{28}O_6Cl_2Cu$ requires C, 56·5; H, 4·7%).

Reaction of α-Acetyl-4-chloroisobutyrophenone with Sodium.—The diketone (8·1 g.) in dry

[12] Ref. 10, p. 482.
[13] Cf. Beyer and Claisen, *Ber.*, 1887, **20**, 2178.
[14] Claus, *ibid.*, 1886, **19**, 230; Verley, *Bull. Soc. chim. France*, 1897, **17**, 910.
[15] Buu-Hoï, Hoan, and Xuong, *Rec. Trav. chim.*, 1952, **71**, 285.
[16] Bayless and Hauser, *J. Amer. Chem. Soc.*, 1954, **76**, 2306.

XUM

ether (25 c.c.) reacted vigorously with a suspension of powdered sodium (2·0 g.) in dry ether (25 c.c.). After 48 hr. the product was isolated as described above, yielding 4-chloro-α-isobutyrylacetophenone (1-*p*-chlorophenyl-4-methylpentane-1,3-dione) (II; $R^1 = Cl$, $R^2 = R^3 = H$), b. p. (bath) 130—135°/0·05—0·10 mm. (0·5 g.), identical with an authentic specimen (infrared comparison, see below). The copper complex separated from benzene–light petroleum (b. p. 40—60°) in greyish-blue needles, m. p. 230° (decomp., with some previous softening) alone or mixed with an authentic specimen (see below).

4-Chloro-α-isobutyrylacetophenone (cf. preceding paragraph).—4-Chloroacetophenone (15·5 g.) in dry ether (50 c.c.) was added during 10 min. to a vigorously stirred suspension of finely powdered sodamide (10·0 g.) in dry ether (100 c.c.). After 5 min. ethyl isobutyrate (23·2 g.) in dry ether (50 c.c.) was added all at once, and the mixture refluxed on the water-bath for 2 hr., cooled, and poured on ice. The aqueous layer was separated, acidified, and extracted with ether. The extract was washed with sodium hydrogen carbonate solution, dried, and evaporated, yielding *4-chloro-α-isobutyrylacetophenone* (2·5 g.), b. p. 130° (bath)/0·05 mm. (Found: C, 64·4; H, 5·6. $C_{12}H_{13}O_2Cl$ requires C, 64·2; H, 5·8%). It showed an infrared (liquid film) conjugate chelate spectrum, with wide bands in the 3000 and 1600 cm.$^{-1}$ regions. The product gave a wine-red colour with ferric chloride and formed a *copper complex*, greyish-blue needles [from benzene–light petroleum (b. p. 40—60°)], m. p. 230° (decomp., with some previous shrinking) (Found: C, 56·3; H, 4·2. $C_{24}H_{24}O_4Cl_2Cu$ requires C, 56·4; H, 4·7%). Alkaline hydrolysis of the diketone afforded *p*-chlorobenzoic acid, m. p. and mixed m. p. 235—236°.

3-Nitroisobutyrophenone.—Isobutyrophenone (29·4 g.) was added during 30 min. with stirring to a mixture of fuming nitric acid (125 c.c.) and acetic anhydride (165 c.c.) [17] at <5°. The mixture was poured on ice and extracted with ether. The extract was washed with sodium hydrogen carbonate solution and water, dried, and evaporated. The residual *3-nitroisobutyrophenone* distilled at 115—118°/0·6 mm. (72%) as a pale yellow oil (Found: C, 61·6; H, 5·5. $C_{10}H_{11}O_3N$ requires C, 62·15; H, 5·7%), $\nu_{max.}$ (liquid film) (C=O) 1680 cm.$^{-1}$. Oxidation of the ketone with boiling 2N-nitric acid gave *m*-nitrobenzoic acid, m. p. and mixed m. p. 140°. The *2,4-dinitrophenylhydrazone* separated from ethanol in orange prismatic needles, m. p. 132° (Found: C, 51·5; H, 4·25. $C_{16}H_{15}O_6N_5$ requires C, 51·5; H, 4·1%). The *p-nitrophenylhydrazone* crystallised from ethanol in brown needles, m. p. 141·5—142° (Found: C, 58·8; H, 4·8. $C_{16}H_{16}O_4N_4$ requires C, 58·5; H, 4·9%).

α-Acetyl-3-nitroisobutyrophenone (I; $R^1 = R^3 = H$, $R^2 = NO_2$).—The acetylation of 3-nitroisobutyrophenone (20 g.) with acetic anhydride (21·2 c.c.) and boron trifluoride in the usual manner afforded *α-acetyl-3-nitroisobutyrophenone* (16·7 g.), b. p. 102—105°/0·06 mm. (after two redistillations) (Found: C, 61·7; H, 6·0; N, 6·3. $C_{12}H_{13}O_4N$ requires C, 61·3; H, 5·6; N, 6·0%). $\nu_{max.}$ (liquid film) (C=O) 1690 (conjugated with benzene ring) and 1746 cm.$^{-1}$ (unconjugated). Hydrolysis with 2N-sulphuric acid gave 3-nitroisobutyrophenone and acetic acid. A *mono-2,4-dinitrophenylhydrazone*, prepared in alcoholic sulphuric acid below 15°, separated from ethyl acetate in yellow plates, m. p. 204·5—205° (Found: C, 50·9; H, 4·0. $C_{18}H_{17}O_7N_5$ requires C, 52·1; H, 4·1%). A *mono-4-phenylsemicarbazone* crystallised from 75% aqueous ethanol in pale yellow needles, m. p. 149° (Found: C, 62·3; H, 5·5. $C_{19}H_{20}O_4N_4$ requires C, 62·0; H, 5·5%). The diketone showed no reaction towards powdered sodium, sodamide, or sodium hydride, in dry ether, nor was a reaction initiated by the addition of a trace of ethyl acetate or ethanol.

α-Acetyl-4-methoxyisobutyrophenone (I; $R^1 = OMe$, $R^2 = R^3 = H$).—This diketone was not formed by reaction between acetic anhydride and 4-methoxyisobutyrophenone in the presence of boron trifluoride. 4-Methoxyisobutyrophenone [18] (11·0 g.) in dry ether (10 c.c.) was added dropwise, with swirling, to ethereal 0·25M-sodium triphenylmethyl (250 c.c.) under nitrogen, followed by acetyl chloride (4·9 g.) in ether (10 c.c.). After 1 hour's refluxing, the solution was kept overnight, then water was added and the organic layer separated, dried, and evaporated. The syrupy residue was mixed with an equal volume of methanol, seeded with triphenylmethane, and kept at 0° for several hours. The triphenylmethane was collected and washed with cold methanol. The combined filtrate and washings were freed from solvent by evaporation, and the residue distilled through a short Vigreux column. After a fore-run of unchanged monoketone, *α-acetyl-4-methoxyisobutyrophenone* distilled at 99—100°/0·075 mm. (23%) (Found: C, 71·0; H, 8·1. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%) and had $\nu_{max.}$ (liquid film) (C=O) 1670

[17] Cf. Morgan and Hickinbottom, *J.*, 1921, **119**, 1879.
[18] Sosa, *Ann. Chim.* (*France*), 1940, **14**, 77.

(phenyl conjugated) and 1743 cm.$^{-1}$ (unconjugated). A *monosemicarbazone* crystallised from ethanol in rectangular plates, m. p. 175·5° (Found: C, 60·3; H, 7·5; N, 15·6. $C_{14}H_{19}O_3N_3$ requires C, 60·6; H, 6·9; N, 15·2%).

Reaction of α-Acetyl-4-methoxyisobutyrophenone with Sodium.—When the diketone (6·8 g.) in dry ether (15 c.c.) was added to powdered sodium (1·45 g.) in ether (15 c.c.) a slow reaction took place. After 4 days the mixture was worked up in the usual manner, giving *α-isobutyryl-4-methoxyacetophenone*, b. p. (bath) 143—148°/0·025 mm. (0·2 g.). The product gave a deep red ferric colour and formed a copper complex, but this could not be obtained crystalline; with 2,4-dinitrophenylhydrazine in alcoholic sulphuric acid it gave 4-methoxyacetophenone 2,4-dinitrophenylhydrazone,[19] m. p. and mixed m. p. 221°. Acidification of the sodium hydrogen carbonate washings gave *p*-anisic acid, m. p. and mixed m. p. 182—183°.

α-Isobutyryl-4-methoxyacetophenone (1-p-*Methoxyphenyl-4-methylpentane-1,3-dione*) (II; R^1 = OMe, $R^2 = R^3 = H$).—4-Methoxyacetophenone [11] (6·0 g.) in dry ether (15 c.c.) was added to ethereal 0·2M-sodium triphenylmethyl (160 c.c.), followed by isobutyryl chloride (4·3 g.) in dry ether. After refluxing for 8 hr. the cooled mixture was extracted twice with cold, dilute sodium hydroxide, and the extracts were acidified with dilute hydrochloric acid. The liberated *α-isobutyryl-4-methoxyacetophenone* distilled at 141—150° (bath)/0·01 mm. (0·6 g.) (Found: C, 71·3; H, 7·4. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). It gave a deep red colour with ferric chloride, and formed a copper complex, which separated from benzene–light petroleum (b. p. 60—80°) in bluish-grey irregular prisms, m. p. 155°. With 2,4-dinitrophenylhydrazine in alcoholic sulphuric acid the product afforded 4-methoxyacetophenone 2,4-dinitrophenylhydrazone,[19] m. p. and mixed m. p. 221°.

Reaction of 2-Acetyl-2-methylindan-1-one (V) *with Sodium.*—2-Acetyl-2-methylindan-1-one [1] (9·8 g.) in dry ether (15 c.c.) was added to a suspension of powdered sodium (2·4 g.) in ether. After the vigorous reaction the mixture was kept for 24 hr., then decomposed with ice and worked up in the manner described. 2-Acetoacetyl-2-methylindan-1-one (VII) distilled at 153—154° (bath)/0·2 mm. (2·35 g.) (Found: C, 72·8; H, 6·4. Calc. for $C_{14}H_{14}O_3$: C, 73·0; H, 6·1%). The copper complex crystallised from benzene in dark green prisms, m. p. 147—148° alone or mixed with a specimen of the copper complex of 2-acetoacetyl-2-methylindan-1-one prepared by the acetylation of 2-acetyl-2-methylindan-1-one.[1] The infrared absorption (liquid film) was of conjugate chelate type, with bands at 1710 (C=O), 2630 (chelated OH), and 1607 cm.$^{-1}$ (chelated C=O). With 2,4-dinitrophenylhydrazine a *pyrazole*, separating from ethanol in orange, rectangular plates, m. p. 171° (Found: C, 61·2; H, 4·1; N, 15·2. $C_{20}H_{16}O_5N_4$ requires C, 61·2; H, 4·1; N, 14·3%), was obtained; it was undepressed in m. p. by admixture with an authentic specimen.

In the acetylation of 2-methylindan-1-one with boron trifluoride and acetic anhydride,[1] there was formed in addition to (V) and (VII) an involatile, neutral *product* in small yield. It crystallised from light petroleum (b. p. 60—80°) in rhombic needles, m. p. 113·5° (Found: C, 72·95; H, 5·7. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%). It is almost certainly a nuclear acetylated product, probably 2,6-diacetyl-2-methylindan-1-one.

Reaction of 3,3-Dimethylpentane-2,4-dione (VIII) *with Sodium.*—The diketone was obtained by the boron trifluoride acetylation of isopropyl methyl ketone.[20] After separation from alkali-soluble material it distilled at 84—86°/11 mm. and gave no colour with ferric chloride. The diketone (2·2 g.) in dry ether (10 c.c.) was added gradually to powdered sodium (0·8 g.) in ether (10 c.c.). When the vigorous reaction had ended the product was isolated in the usual manner, to give 5-methylhexane-2,4-dione (IX), b. p. 74°/12 mm. (0·2 g.), which formed a copper complex, m. p. 170—171° (lit.,[20] m. p. 170—171°), identical (mixed m. p.) with the copper complex of authentic diketone obtained by acidification of the alkaline extracts in the acetylation above.[20]

We thank Dr. G. Eglinton (University of Glasgow) and Mr. G. Phillips for the infrared measurements, and the Imperial Smelting Corporation and Imperial Chemical Industries Limited (Dyestuffs Division) for gifts of chemicals.

Department of Chemistry, University College, Cardiff.

[*Received, March 2nd*, 1959.]

[19] "Organic Reagents for Organic Analysis," Hopkin and Williams, Ltd., 2nd edn., 1950, p. 225.
[20] Hauser and Adams, *J. Amer. Chem. Soc.*, 1944, **66**, 345.

XUM

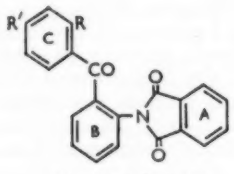
540. *Triazepines. Part I.* 1,2,4-*Triazacyclohepta*-2,5,7-*trienes.*

By (Miss) E. J. Engels, M. Lamchen, and A. J. Wicken.

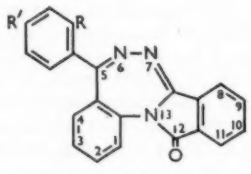
2,4-Dimethoxy- (Ia) and 4-methoxy-2′-phthalimidobenzophenone (Ib) with hydrazine in boiling alcohol give products whose chemical and spectral properties indicate that they are 1,2,4-triazacyclohepta-2,5,7-trienes (II). In contrast, with this, 4-methoxy-2′-phthalimidodiphenylmethane is decomposed by hydrazine according to the Ing and Manske reaction. 2-Phthalimidobenzophenone, β-phthalimidopropiophenone, and 2,4-dimethoxy-β-phthalimidopropiophenone also undergo the normal Ing and Manske decomposition by hydrazine.

Only a few triazacycloheptatrienes (triazepines) have been reported, mainly as di-, tetra-, or hexa-hydro- or benzo-derivatives. The 1,3,5-triaza-system has received most attention; 1,2,5-, 1,3,6-, and 2,3,4-triaza-systems have also been reported, but not investigated. Before our short communication [1] no 1,2,4-triazacycloheptatriene had been reported, though reduced derivatives had been referred to in three instances,[2] but not fully investigated.

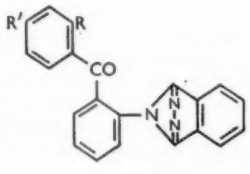
The tosyl group proving difficult to remove in our experiments, we used the phthaloyl group to protect the amino-group of anthranilic acid during a Friedel–Crafts condensation with dimethylresorcinol. 2,4-Dimethoxy-2′-phthalimidobenzophenone (Ia) was then obtained readily and in good yield. When we attempted to remove the phthaloyl group by refluxing an alcoholic suspension of the phthalimide (Ia) with hydrazine,[3] the phthalimide slowly dissolved whilst white needles (A) crystallised. Analysis showed that the



(Ia): R = R′ = OMe
(Ib): R = H, R′ = OMe
(Ic): R = R′ = H



(IIa): R = R′ = OMe
(IIb): R = H, R′ = OMe



(III)

product contained both the nitrogen atoms of the hydrazine, and we suggested [1] that the product formed had structure (IIa).

A structure such as (III; R = R′ = OMe) is unlikely on the basis of known stable bond angles and since its formation should not be affected by groups on ring C (see I) as has been shown to be the case.[1]

Compound A could not be acetylated, contained no active hydrogen, and was stable to refluxing 10N-hydrochloric acid or 5N-sodium hydroxide. These results eliminate a monohydrazone grouping $=N\cdot NH_2$. The molecular weight (microebullioscopic in chloroform [4]) was 368, in good agreement with the structure (IIa).

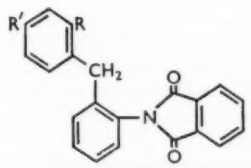
Replacement of the benzophenone-carbonyl group by a methylene group should prevent condensation with hydrazine to a product of type (II). Since it was found that *o*-phthalimidobenzoic acid was readily reduced to *N*-*o*-carboxyphenylphthalimidine by Clemmensen's method, 2,4-dimethoxy-2′-phthalimidodiphenylmethane (IVa) could

[1] Engels, Lamchen, and Wicken, *Proc. Chem. Soc.*, 1958, 191.
[2] Tingle and Bates, *Amer. Chem. J.*, 1914, **36**, 260; Busch, *Ber.*, 1894, **27**, 2901; Losse and Uhlig, *Chem. Ber.*, 1957, **90**, 257.
[3] Ing and Manske, *J.*, 1926, 2348.
[4] Sucharda and Bobranski, "Elementary Analysis of Organic Compounds," Gallenkamp and Co. Ltd., London, 1936, p. 34.

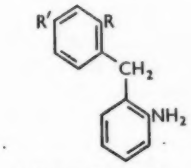
not be prepared directly from the corresponding benzophenone, so we attempted to prepare 2-amino-2′,4′-dimethoxydiphenylmethane (Va).

However, the intermediate 2-amino-2′,4′-dimethoxybenzophenone (VIa) could be obtained only in very small yield. Friedel–Crafts reaction of dimethylresorcinol and the chloride of *N*-toluene-*p*-sulphonylanthranilic acid gave the expected benzophenone, but hydrolysis of the amide group gave only small yields of the amino-compound (VIa) mixed with sulphonated products. Hofmann degradation of 2-(2,4-dimethoxybenzoyl)benzamide was unsuccessful. Similarly 2-(2,4-dimethoxybenzyl)benzoic acid, prepared as described by Tambor,[5] was converted into the amide but could not be degraded to the amine (Va) by the Hofmann degradation (hypobromite or hypochlorite), the Schmidt reaction, or the Curtius reaction.

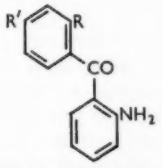
Then, 4-methoxy-2′-phthalimidobenzophenone (Ib), obtained from a Friedel–Crafts reaction of *o*-phthalimidobenzoyl chloride with anisole, on treatment with hydrazine gave a condensation product which, as it was analogous to compound (A), we considered to have structure (IIb). So attempts were made to prepare 4-methoxy-2′-phthalimidodiphenyl-



(IVa): R = R′ = OMe
(IVb): R = H, R′ = OMe



(Va): R = R′ = OMe
(Vb): R = H, R′ = OMe



(VIa): R = R′ = OMe
(VIb): R = H, R′ = OMe

methane (IVb). 2-Amino-4′-methoxybenzophenone (VIb) was readily obtained by the method of Simpson *et al.*;[6] its reduction was however dependent on the method used. Zinc dust in alkali, Clemmensen reduction, Wolff–Kishner reduction, and the Huang-Minlon[7] modification thereof, failed to give the expected product. Catalytic hydrogenation with palladium–charcoal failed, but with Adams catalyst one mol. of hydrogen was absorbed. This suggested reduction to the alcohol only, and although this oily product was not obtained pure it formed a picrate which gave correct analyses for the alcohol. This was surprising since Hartung and Crossley[8] found that palladium–charcoal was effective for reduction of propiophenones, and that no hydrogenation took place with platinised charcoal; they further found that this hydrogenation did not appear to proceed via the alcohol. The method of Hewett *et al.*[9] of reducing *o*-aminobenzophenone with sodium in ethanol was found to give good yields of the diphenylmethane (Vb); fusion of this with phthalic anhydride gave the phthalimide (IVb).

Refluxing a suspension of the imide (IVb) in ethanol with hydrazine produced phthalhydrazide and the free amine (Vb), and no condensation product, as expected.

Models (" Catalin ") showed that the suggested structure (II) would, with some slight strain, fit the normal valency angles. The triazepine ring is however buckled, and the phenyl group B (see II) projects at an angle from a planar ring-system. Structure (II), however, has many canonical forms (VII, where * indicates possible positions of the positive charge); some of which produce completely planar structures, *e.g.*, (VIII) and (IX); (VIII), with complete aromaticity, is probably the most important. The high degree of resonance also accounts for the great stability of the compound.

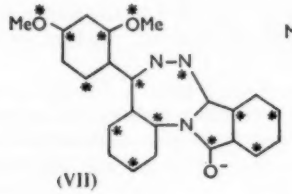
Models further indicated that 3- and 4-phthalimidobenzophenones could not form

[5] Tambor, *Ber.*, 1910, **43**, 1886.
[6] Simpson, Atkinson, Schofield, and Stephenson, *J.*, 1945, 646.
[7] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.
[8] Hartung and Crossley, *ibid.*, 1934, **56**, 158.
[9] Hewett, Lermit, Openshaw, Todd, Williams, and Woodward, *J.*, 1948, 292.

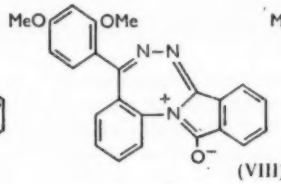
XUM

similar condensation products since the =N–N= group could not bridge the benzophenone- and the phthalimido-carbonyl group. 2,4-Dimethoxy-3'- and -4'-phthalimidobenzophenone were prepared by Friedel–Crafts reactions from *m*- and *p*-phthalimidobenzoyl chloride respectively with dimethylresorcinol, and on treatment with hydrazine both gave the normal Ing and Manske decomposition.

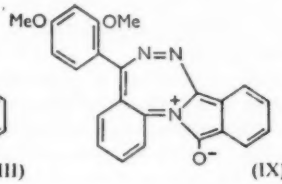
A structure such as (VIII) should confer colour on the compound. Our products are colourless; but although there is practically no absorption down to 400 mμ, there is a



(VII)



(VIII)



(IX)

rapid rise in ε just outside the visible region, and at 380 mμ log ε exceeds 4, and it retains this value to the limit of our determination (225 mμ). A few broad peaks and one sharp peak are found above this general plateau. The positions of the absorption bands, both ultraviolet and infrared, of compounds considered as (IIa and b) are almost identical, confirming the similarity of structure.

Infrared spectra of compounds were consistent with the suggested structures (IIa and b) and excluded all alternatives. No benzophenone-carbonyl absorption and no N–H stretching vibration of a primary or secondary amino-group is present. A phthalimido-group should show two absorption bands, arising from the two carbonyl groups; the compounds (IIa and b) have only one absorption band (at 1712 cm.$^{-1}$) corresponding to a single αβ-unsaturated carbonyl group located in a five-membered ring (1716 cm.$^{-1}$).[10]

When 2-phthalimidobenzophenone (Ic), prepared by fusion of 2-aminobenzophenone with phthalic anhydride, was similarly treated with hydrazine no triazepine was formed; instead, the normal Ing and Manske decomposition give almost quantitative yields of 2-aminobenzophenone and phthalhydrazide. The substituents on ring c thus influence the course of the reaction.

To obtain information about the mechanism and the scope of the condensation, other phthalimidophenones with the grouping ·CO·C·C·N·CO· were prepared. β-Phthalimidopropiophenone, and 2,4-dimethoxy-β-phthalimidopropiophenone were prepared by Friedel–Crafts condensation of 3-phthalimidopropionyl chloride with benzene and dimethylresorcinol respectively. With hydrazine in boiling alcohol these underwent the normal decomposition to phthalhydrazide, and no condensation product could be isolated from 2-benzamido-5-methylbenzophenone.

The initial reaction of hydrazine with β-phthalimidopropiophenone and 2,4-dimethoxy-β-phthalimidopropiophenone must have been on a phthalimido-carbonyl group as phthalhydrazide was produced in both cases. It can thus be assumed that since 2-phthalimidobenzophenone also produced phthalhydrazide the initial attack here and thus on 2,4-dimethoxy-2'-phthalimidobenzophenone, which produced the triazepine, was also on a carbonyl group of the phthalimido-residue. Electron-repelling *ortho*- and/or *para*-groups in ring c could activate the benzophenone-carbonyl group sufficiently to make it react with the NH_2-group of the hydrazide formed provided other factors are favourable, and provided the initial attack is an electrophilic attack on the oxygen atom. Activation, in this sense, of the carbonyl group alone is not sufficient to effect triazepine formation since

[10] Bellamy, " The Infra-Red Spectra of Complex Molecules," Methuen and Co. Ltd., London, 2nd edn., 1958, p. 149; Jones, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 956; Fuson, Josien, and Shelton, *ibid.*, 1954, **76**, 2526.

2,4-dimethoxy-β-phthalimidopropiophenone gave the normal Ing and Manske decomposition.

Stereochemical effects may be operative since the substitution of a $\cdot CH_2 \cdot CH_2 \cdot$ chain, as in 2,4-dimethoxy-β-phthalimidopropiophenone, for an *ortho*-phenylene group in 2,4-dimethoxy-2'-phthalimidobenzophenone (Ia) caused decomposition instead of triazepine formation.

Experimental

2,4-Dimethoxy-2'-phthalimidobenzophenone.—Phthaloylanthranilic acid (10 g.) and phosphorus pentachloride (8 g.) were refluxed in dry carbon disulphide (50 ml.) until evolution of hydrogen chloride ceased (2½ hr.). Dimethylresorcinol (6 g.) was added to the cooled solution, and then anhydrous aluminium chloride (12·5 g.) in small portions during 30 min.; a dark red precipitate was formed. After refluxing (1½ hr.), the carbon disulphide was decanted and the complex decomposed with hydrochloric acid and ice. The product was washed with dilute hydrochloric acid, then with water, and finally with a little ethanol which removed most of the impurities. The residue was treated with charcoal in acetic acid, and recrystallised from dilute acetic acid, to yield *2,4-dimethoxy-2'-phthalimidobenzophenone* (8 g., 55%) as colourless rods, m. p. 231—232° (Found: C, 71·6; H, 4·4; OMe, 15·6. $C_{23}H_{17}O_5N$ requires C, 71·3; H, 4·4; OMe, 16·0%). The compound is soluble in glacial acetic acid, acetone, benzene, and hot ethanol, only slightly in cold ethanol, and insoluble in water and ether.

5-(2,4-Dimethoxyphenyl)-12-oxobenzo[5,6]-1,2,4-triazepino[3,4-a]isoindole (IIa).—2,4-Dimethoxy-2'-phthalimidobenzophenone (2 g.) was suspended in ethanol (40 ml.), aqueous 95% hydrazine (0·3 ml.) added, and the mixture refluxed. After about 30 min. fine white needles crystallised, while the starting material slowly dissolved. Refluxing was continued for 30 min. after no more starting material could be seen (total 4 hr.), then the mixture was cooled and filtered. The *product* melted at 271—272°, this m. p. being unchanged by recrystallisation from chloroform (yield, 1·9 g., 95%) (Found: C, 72·1; H, 4·5; N, 10·7; OMe, 15·6. $C_{23}H_{17}O_3N_3$ requires C, 72·1; H, 4·4; N, 11·0; OMe, 16·2%); $\lambda_{max.}$ were at 342, 328, 305, 283, and 230 mμ (log ε 4·13, 4·14, 4·15, 4·48, and 4·56); $\nu_{max.}$ (in Nujol) were at 1712 vs, 1612, 1579, 1552, 1514, 1490, and 1473 $cm.^{-1}$. The compound is insoluble in water, alkali, mineral acid, ether, ethanol, and most organic solvents, but soluble in hot chloroform, pyridine, the higher alcohols, and glacial acetic acid.

2-Phthalimidobenzophenone.—2-Aminobenzophenone (0·7 g.) and phthalic anhydride (0·5 g.) were fused together at 180—200°. The cooled melt was extracted with ethanol (charcoal), and on dilution crystallised. Recrystallisation from dilute ethanol yielded *2-phthalimidobenzophenone*, m. p. 198—199° (Found: C, 76·9; H, 3·9; N, 4·3. $C_{21}H_{13}O_3N$ requires C, 77·1; H, 4·0; N, 4·3%).

Reaction with Hydrazine.—2-Phthalimidobenzophenone (0·3 g.) was refluxed with aqueous 95% hydrazine (4 drops) in ethanol (10 ml.). The solution became yellow and crystals were precipitated within a few minutes. After refluxing (4 hr.) the solution was cooled; the crystals were filtered off and recrystallised from ethanol to yield phthalhydrazide, m. p. 333—334°. The alcoholic solution was evaporated, the residue taken up in ether, and the ether solution evaporated to dryness; the residue obtained on recrystallisation from dilute ethanol yielded 2-aminobenzophenone (0·17 g., 94%), m. p. and mixed m. p. 103—105°.

2,4-Dimethoxy-β-phthaloylpropiophenone.—β-Phthalimidopropionic acid (10 g.) and phosphorus pentachloride (9·5 g.) were refluxed in dry carbon disulphide (50 ml.) for 1½ hr. To the cooled solution was added dimethylresorcinol (7 g.), and then powdered aluminium chloride (16 g.) was added during 30 min. The whole was refluxed for 1½ hr. The purple sticky solid complex was decomposed with ice and hydrochloric acid, and the excess of dimethylresorcinol and carbon disulphide were removed in steam. The solid residue was washed with aqueous sodium hydrogen carbonate, and recrystallised from ethanol, to yield *2,4-dimethoxy-β-phthalimidopropiophenone* (7 g., 52%) as needles, m. p. 151—152° (Found: C, 66·9; H, 5·2. $C_{19}H_{17}O_5N$ requires C, 67·2; H, 5·0%), soluble in most organic solvents but insoluble in water, acids, and alkalis.

Refluxing this compound in alcoholic suspension with hydrazine gave phthalhydrazide within a short time.

Reaction of Hydrazine with 2-Benzamido-5-methylbenzophenone.—2-Benzamido-5-methylbenzophenone (0·6 g.) was refluxed with 95% aqueous hydrazine (1 equiv.) in ethanol (40 ml.)

XUM

for 6 hr. Nothing separated and on evaporation of the pale yellow solution a yellow gum was obtained from which no condensation product could be isolated; only small amounts of an acid-soluble substance, which could not be purified, were isolated.

4-Methoxy-2′-phthalimidobenzophenone.—*o*-Phthalimidobenzoic acid (10 g.) was refluxed with phosphorus pentachloride (8 g.) in anhydrous *sym*-tetrachloroethane (100 ml.) until evolution of hydrogen chloride had practically ceased (1½ hr.). After cooling, dry anisole (4·6 g.) was added and then aluminium chloride (13 g.) during 30 min. A deep purple solution was produced in a marked exothermic reaction. The mixture was heated at 40—50° for 1½ hr. and left at room temperature for a further 1½ hr. before decomposition with ice and hydrochloric acid. Solvent and unchanged anisole were removed by steam-distillation, and the crude solid residue was recrystallised (charcoal) from dilute acetic acid, to yield *4-methoxy-2′-phthalimidobenzophenone* as fine needles (10·2 g., 76%), m. p. 206—207° (Found: C, 73·6; H, 4·3; N, 3·9. $C_{22}H_{15}O_4N$ requires C, 73·9; H, 4·2; N, 3·9%). Condensation in carbon disulphide gave only a 32% yield.

5-p-Methoxyphenyl-12-oxobenzo[5,6]-1,2,4-*triazepino*[3,4-a]*isoindole* (IIb).—4-Methoxy-2′-phthalimidobenzophenone (1 g.) was suspended in ethanol (40 ml.), aqueous 95% hydrazine (0·15 ml.) added, and the mixture refluxed, with two further additions of hydrazine (0·05 ml. each) at hourly intervals. Within 1 hr. all starting material was dissolved; then needles soon separated. After 4 hours' refluxing, the solution was cooled and filtered, and the needles were washed with ethanol to give the *product*, (0·9 g., 91%), m. p. 241—242°. Recrystallisation from glacial acetic acid did not change the m. p. (Found: C, 74·4; H, 4·25; N, 11·7. $C_{22}H_{15}O_2N_3$ requires C, 74·8; H, 4·25; N, 11·9%). $\lambda_{max.}$ were at 347, 306, 291, and 233 mμ (log ε 4·13, 4·38, 4·45, and 4·55), and $\nu_{max.}$ (in Nujol) at 1712 vs 1612, 1579, 1550, 1519, 1488, 1470 cm.$^{-1}$.

Reduction of 2-Amino-4′-methoxybenzophenone.—(a) *Catalytic.* In presence of Adams catalyst (0·3 g.) in ethanol (100 ml.) 2-amino-4′-methoxybenzophenone (2·9 g.) absorbed 1 mol. of hydrogen under 3 atm. in 20 hr. After filtration, the filtrate was evaporated to give a yellow oil. Formed in, and recrystallised from, ethanol *o-aminophenyl-p-methoxyphenylmethanol picrate* had m. p. 151·5—153·5° (Found: C, 52·8; H, 3·5; N, 12·4. $C_{20}H_{18}O_9N_4$ requires C, 52·4; H, 4·0; N, 12·4%).

(b) *With sodium in ethanol.* 2-Amino-4′-methoxybenzophenone (5 g.), in ethanol (50 ml.), was added rapidly to sodium wire (5 g.). The vigorous reaction was allowed to proceed unchecked. Later, more hot ethanol (20 ml.) was added and the mixture warmed till the sodium had dissolved. The hot solution was diluted with water (250 ml.), and the alcohol removed by steam-distillation. The remaining solution was extracted with ether, the ether evaporated, and the solid residue taken up in benzene (10 ml.). Concentrated hydrochloric acid (10 ml.) was added to this solution and, on chilling in ice, the solid hydrochloride of the amine separated. It was washed with benzene, dried, and dissolved in hot water. This solution was made alkaline with ammonia and extracted with ether. Evaporation yielded an oil (3·5 g.) which solidified. Recrystallising a small amount from light petroleum yielded 2-amino-4′-methoxydiphenylmethane as needles, m. p. 52—55°. The crude amine (1 g.) was fused with phthalic anhydride (0·7 g.) at 180—200° for 20 min. Recrystallising the solid obtained on cooling from dilute ethanol yielded *4-methoxy-2′-phthalimidodiphenylmethane* (1 g., 62%) as plates, m. p. 142—145° (Found: C, 76·7; H, 5·0; N, 3·95. $C_{22}H_{17}O_3N$ requires C, 76·9; H, 3·0; N, 4·1).

Refluxing this phthalimido-compound with hydrazine in ethanol yielded phthalhydrazide and the free amine.

2,4-Dimethoxy-3′-phthalimidobenzophenone.—*m*-Phthalimidobenzoic acid (10 g.), phosphorus pentachloride (8 g.), and anhydrous *sym*-tetrachloroethane (75 ml.) were refluxed together till evolution of hydrogen chloride ceased (1 hr.). To the cooled solution was added dimethylresorcinol (6 g.), then aluminium chloride (12·5 g.) during 30 min. When the reaction subsided, the mixture was heated at 50° for 1 hr. and decomposed with ice and hydrochloric acid. The solid obtained, after removal of the solvent and excess of dimethylresorcinol in steam, was recrystallised (charcoal) from acetic acid, to yield *2,4-dimethoxy-3′-phthalimidobenzophenone* (9 g., 62%) as needles with a pale iridescent emerald colour, m. p. 166—168° (Found: C, 70·9; H, 4·5; N, 3·5. $C_{23}H_{17}O_5N$ requires C, 71·3; H, 4·4; N, 3·6%).

This benzophenone (2 g.) was refluxed with ethanol (40 ml.) and 95% hydrazine solution (0·5 ml.). The solution became yellow immediately and after 30 min. phthalhydrazide (identified by m. p. and mixed m. p.) separated.

p-*Phthalimidobenzoic Acid.*—*p*-Aminobenzoic acid (10 g.) and phthalic anhydride (10·8 g.) were refluxed in glacial acetic acid (120 ml.) for 1 hr. The mixture was poured into excess of water, and the solid filtered off, washed with water, and recrystallised from 96% ethanol to give p-*phthalimidobenzoic acid* (15 g., 77%) as needles, m. p. 285—287° (Found: C, 67·2; H, 3·3; N, 5·1. $C_{15}H_9O_4N$ requires C, 67·4; H, 3·4; N, 5·2%).

2,4-*Dimethoxy-4'-phthalimidobenzophenone.*—Starting with *p*-phthalimidobenzoic acid (10 g.), using the same reagents and procedure as for the 3-phthalimidobenzophenone, and recrystallisation from acetic acid yielded 2,4-*dimethoxy-4'-phthalimidobenzophenone* (9 g., 62%) as needles with a pale emerald colour, m. p. 185—187° (Found: C, 70·8; H, 4·6; N, 3·5. $C_{23}H_{17}O_5N$ requires C, 71·3; H, 4·4; N, 3·6%).

When the benzophenone (2 g.) and 95% aqueous hydrazine (0·5 ml.) in ethanol (40 ml.) were refluxed, phthalhydrazide (identified by m. p. and mixed m. p.) was precipitated in 30 min.

The authors thank Sir Alexander Todd for allowing infrared spectra to be taken in his laboratory and Dr. N. Shephard for discussions thereof.

Department of Chemistry, University of Cape Town, Cape Town, South Africa. [*Received, February 16th*, 1959.]

---

541. *Stereoisomerism of Addition Polymers. Part III.*[1] *The Optical Rotatory Power of Poly[(+)-1 : 3-Dimethylbutyl Methacrylate] and of Copolymers with Methyl Methacrylate.*

By C. L. Arcus and D. W. West.

Polymers of (+)-1 : 3-dimethylbutyl methacrylate, and copolymers with methyl methacrylate, have been prepared, and the rotatory power of their solutions in *sym*-tetrachloroethane measured. Change in concentration of solutions, in molecular weight, and from benzoyl peroxide to αα'-azoisobutyronitrile as initiator, have little effect on optical rotation.

The use of molecular-rotation differences leads to the conclusion that dissymmetric secondary coiling of the main chain in these polymers contributes to the rotatory power.

In furtherance of a study of addition-polymer stereoisomerism, a theoretical treatment of which was given earlier,[1,2] the optical rotatory powers of a group of polymethacrylates have been investigated and related to aspects of molecular structure. References in the literature to optically active polymers have been discussed in Part II; to these is added the preparation and polymerisation of (+)-s-butyl α-chloroacrylate.[3] In no case were the authors primarily interested in rotatory power, and values for only a single wavelength and concentration are usually given for each polymer specimen.

In the present work (+)-1 : 3-dimethylbutyl methacrylate has been prepared by the reaction of methacryloyl chloride with (+)-1 : 3-dimethylbutanol. This alcohol was selected because its rotatory dispersion in the visible region is simple, and it is of low molecular weight and can readily be resolved;[4] further, the (±)-methacrylate had earlier been prepared and polymerised by Crawford.[5] The (+)-methacrylate was polymerised by initiation with benzoyl peroxide, and the rotatory power to visible light of five wavelengths determined. Similar measurements have been made on polymer initiated with αα'-azoisobutyronitrile, and on copolymers of the (+)-methacrylate with methyl methacrylate. Solutions in *sym*-tetrachloroethane have been used throughout.

In order to apply the method of molecular-rotation differences, (+)-1 : 3-dimethylbutyl

[1] Part II, Arcus, *J.*, 1957, 1189.
[2] Part I, Arcus, *J.*, 1955, 2801.
[3] Crawford and Plant, *J.*, 1952, 4492.
[4] Kenyon and Strauss, *J.*, 1949, 2153.
[5] Crawford, *J. Soc. Chem. Ind.*, 1949, **68**, 201.

pivalate has been prepared. Differences have been determined for the series of five wavelengths, in preference to the use of a single wavelength, in order to provide a check on the possible incidence of anomalous dispersion.

Experimental

Rotations are at 25°; those of undiluted liquid compounds are for *l* 1·0, and those of solutions for *l* 2·0, unless otherwise stated.

Pyridine, dried with, then distilled from, potassium hydroxide, was passed down a column of alumina in order to remove peroxides.

sym-Tetrachloroethane (400 ml.) was repeatedly stirred with 50 ml. portions of sulphuric acid, with heating on a steam-bath, then steam-distilled, dried ($CaCl_2$), and distilled; it had b. p. 144—146°, d_4^{25} 1·587.

Methacryloyl chloride, b. p. 96—98°, and pivaloyl chloride, b. p. 105—106°, were prepared by the reaction of methacrylic acid (b. p. 100°/70 mm.) with benzenesulphonyl chloride, and of pivalic acid (b. p. 165°) with benzoyl chloride, according to directions by Heyboer and Staverman [6] and Brown [7] respectively.

(±)-1 : 3-Dimethylbutanol was dried (K_2CO_3) and distilled through a Vigreux column; it had b. p. 128—130°. Three resolutions by Kenyon and Strauss's method [4] yielded (+)-1 : 3-dimethylbutanol having α_{5893}^{24} +16·76°, α_{5893} +16·58°, α_{5893} +16·80°.

Pivaloyl chloride (9·6 g.) was added to an ice-cold mixture of pyridine (12·6 g.) and (+)-1 : 3-dimethylbutanol (8·2 g.) containing a little copper powder. The whole was boiled for 1½ hr.; after cooling, it was added to dilute hydrochloric acid. The product was extracted with light petroleum (b. p. 40—60°) and twice distilled, yielding (+)-1 : 3-*dimethylbutyl pivalate* (11·8 g.), b. p. 77—78°/22 mm., n_D^{23} 1·4070, α_{5893}^{24} 19·59° (Found: C, 70·8; H, 11·65. $C_{11}H_{22}O_2$ requires C, 70·9; H, 11·9%).

Methacryloyl chloride (17·3 g.) was added to an ice-cold, stirred mixture of (+)-1 : 3-dimethylbutanol (16·3 g.), pyridine (15·8 g.), and t-butylcatechol (0·4 g.). The mixture was kept at 85° for 5 min. and kept overnight at 25°, then poured into hydrochloric acid (4·5 ml.) and water (160 ml.). The whole was thrice extracted with light petroleum (b. p. 40—60°), and the extract was thrice washed with 0·5N-sodium hydroxide, then with water, and dried ($MgSO_4$). The product from evaporation of the extract was twice distilled, quinol (0·28 g.) being added on evaporation and before the second distillation, and yielded (+)-1 : 3-*dimethylbutyl methacrylate* (average yield 49%), b. p. 75—78°/20 mm., n_D^{25} 1·4224, α_{5893} 34·77° (Found: C, 70·15; H, 10·75. $C_{10}H_{18}O_2$ requires C, 70·55; H, 10·65%).

Partially active (−)-1 : 3-dimethylbutanol having α_{5893} −10·33° similarly gave (−)-1 : 3-dimethylbutyl methacrylate, b. p. 70—71°/14 mm., α_{5893} −21·69°.

Polymerisations.—In each instance the polymer or copolymer was a hard, colourless, glass. The specimen was crushed, and kept at 1 mm., at room temperature for the fully active, and at 75° for the other specimens, until the weight was constant; the losses were small.

(1 and 2) (+)-1 : 3-Dimethylbutyl methacrylate, containing 0·01% of benzoyl peroxide, was heated under nitrogen as follows: (1) at 82°, 30 min.; 45°, 80 hr.; 110°, 5 hr. (2) at 85°, 1 hr.; 79°, 25 hr. For specimen (1) there was found C, 71·1; H, 10·8%. Part of the surface of specimen (2) had become white, opaque, and readily detachable; it was thought that this material might be crystalline: however, it appeared amorphous under the microscope, and an *X*-ray crystallographic examination (for which we thank Dr. C. W. Bunn, Imperial Chemical Industries Limited, Plastics Division) showed only amorphous polymer to be present; its identity was checked by analysis (Found: C, 70·4; H, 10·9%).

(3) (−)-1 : 3-Dimethylbutyl methacrylate (3·4 g.) containing benzoyl peroxide (0·0068 g.) was heated under nitrogen at 79° for 5 hr.

(4) A similar polymerisation was carried out, but the benzoyl peroxide was replaced by the equimolar quantity of αα′-azoisobutyronitrile (0·0059 g.). Polymers (3) and (4) were lævorotatory, but, to facilitate comparison of molecular rotations, are recorded as dextrorotatory in Table 1.

(5) (+)-1 : 3-Dimethylbutyl methacrylate (3·41 g.), methyl methacrylate (b. p. 40—41°/100

[6] Heyboer and Staverman, *Rec. Trav. chim.*, 1950, **69**, 787.
[7] Brown, *J. Amer. Chem. Soc.*, 1938, **60**, 1325.

mm.; 4·10 g.), and αα′-azoisobutyronitrile (0·075 g.) were warmed and stirred until homogeneous, the air was then displaced by nitrogen and the whole heated at 76° for 100 min. (Found: C, 64·3; H, 9·25. Calc. for $C_5H_8O_2 : C_{10}H_{16}O_2 = 2·33 : 1$: C, 64·45; H, 9·15%).

(6) Copolymer was similarly prepared from methyl methacrylate (6·00 g.), (+)-1 : 3-dimethylbutyl methacrylate (3·43 g.), and αα′-azoisobutyronitrile (0·093 g.) (Found: C, 63·8; H, 8·85. Calc. for $C_5H_8O_2 : C_{10}H_{16}O_2 = 3·20 : 1$: C, 63·65; H, 8·95%).

The preparation of polymer solutions of known, and relatively high, concentrations presented some difficulty, owing to the time required for dissolution and to the high viscosity of the solutions; the following method was evolved. Polymer (1 g.) and *sym*-tetrachloroethane (20 ml.) were placed in a boiling-tube, which was connected by a ground joint to a vertical tube, surrounded by a water-jacket, through which passed a loosely fitting stirrer. The boiling-tube was placed in a cylindrical recess in a flask, fitted with a reflux condenser, containing boiling butan-1-ol (b. p. 116°). Stirring and heating were continued until dissolution was complete. The density of the solution at 25° was determined. At first, concentration was determined by evaporation of a known weight of solution, followed by heating at 80° to constant weight. Subsequently, and more conveniently, the water-jacket, above, was made a separate unit (a long torus) sliding on to the vertical tube; it was then practicable to weigh accurately the boiling-tube and contents with the vertical tube and stirrer, and so to ascertain the weight of solution containing a known weight of polymer. A comparison of the two methods with the same solution gave *c* 4·96 and 5·03 (g. of polymer in 100 ml. solution) respectively.

TABLE 1. *Rotatory powers of polymers and copolymers of* (+)-1 : 3-*dimethylbutyl methacrylate and of* (+)-1 : 3-*dimethylbutyl pivalate in* sym-*tetrachloroethane at* 25°.

Compound	Solution no.	*c*	Rotation	Rotation * at λ (Å) 6438	5893	5461	5086	4358
Fully active polymer (1) ...	i	4·79	[α]	14·2°	18·0°	20·2°	24·2°	—
	ii	5·01	[α]	14·4	17·7	20·2	24·3	33·4°
	iii	6·63	[α]	13·9	18·3	—	25·2	34·7
	iv	7·19	[α]	15·0	17·3	21·4	25·3	34·9
			[*M*]	24·3	30·3	34·4	41·3	56·8
Fully active polymer (2) ...	i	4·96	[α]	14·5	18·0	21·1	24·8	33·2
	ii	4·88	[α]	14·8	18·2	20·8	24·8	33·5
			[*M*]	24·9	30·9	35·6	42·2	56·7
Pivalate	i	4·71	[α]	20·5	23·4	26·8	31·3	44·0
	ii	4·74	[α]	20·2	23·3	26·8	31·0	44·3
			[*M*]	37·9	43·5	49·8	58·0	82·3
			$[M]_s$	−13·0	−12·6	−14·2	−15·8	−25·6
Partially active polymer (3)	i	4·93	[α]	9·6	11·1	12·7	14·8	20·5
	ii	4·85	[α]	9·4	10·8	12·5	14·9	20·7
Partially active polymer (4)	i	4·87	[α]	9·0	11·1	13·3	15·3	20·9
	ii	4·81	[α]	9·2	11·2	13·0	15·5	20·3
			$[M]_{sn}$	1·3	−0·5	−0·4	−0·5	0·4
Copolymer (5)	i	5·27	[α]	6·3	8·8	10·1	11·9	16·6
	ii	5·17	[α]	7·0	8·7	10·3	11·7	15·5
			$[M]_{sn}$	1·1	2·2	3·0	2·8	3·5
Copolymer (6)	i	5·33	[α]	5·0	6·8	8·3	9·6	12·5
	ii	5·14	[α]	6·0	7·0	8·1	9·8	12·4
			$[M]_{sn}$	0·8	1·0	1·7	1·8	1·1

* Positive unless otherwise stated.

TABLE 2.

Polymer or copolymer no.	1	2	3	4	5	6
c	0·657	0·345	0·621	0·614	0·674	0·682
$[\eta]_c$	0·99	2·21	0·95	0·51	0·29	0·26

In Table 1, the molecular rotations are calculated from the average of the specific rotation (at *c* 5); the values for polymers (3) and (4) have been combined.

The intrinsic viscosity, $[\eta]_c = (1/c) \ln (\eta_{soln.}/\eta_{solv.})$, of a solution of the polymer or copolymer in *sym*-tetrachloroethane was determined at 25°.

Results and Discussion

Since little is known of the optical rotatory properties of solutions of polymers bearing optically active groups, the effect on rotation of change of concentration, initiator, and molecular weight has been investigated.

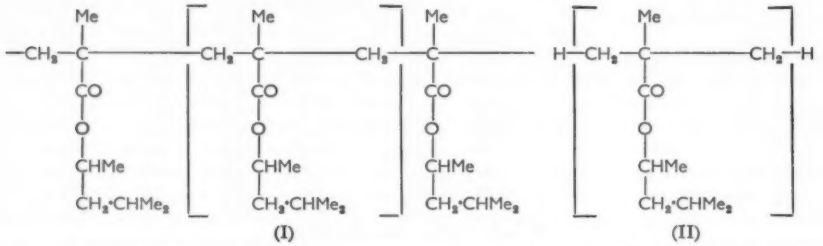
With respect to fully active poly[(+)-1 : 3-dimethylbutyl methacrylate] [polymer (1), Table 1], variation of c from 4·79 to 7·19, the last value approaching the limit of solubility of the polymer, resulted in no significant change in the specific rotations.

A specimen of (+)-1 : 3-dimethylbutyl methacrylate (61·5% optically pure) was polymerised by initiation with benzoyl peroxide and with αα′-azoisobutyronitrile. The rotatory powers of the two polymers [(3) and (4), Table 1] are seen to be substantially the same, indicating that the steric course of polymerisation is unaffected by the nature of the radicals initiating the reaction. Further, the change in molecular weight corresponding to a doubling in intrinsic viscosity does not significantly alter the specific rotations [polymers (1) and (2), and (3) and (4), Tables 2 and 1].

It is necessary, in the present discussion, to use the distinction which has been made [8] between the primary and the secondary structure of a macromolecule. The former is the covalent structure of the polymer considered apart from the chain-coiling due to steric or other non-covalent interactions of the side groups, and for the present polymers is exemplified in formula (I). The secondary structure is the form of helical coiling which the polymer chain takes up in any given circumstance; it is a conformation, not a configuration.

The following treatment, which is provisional, provides an analysis of the rotatory power of the polymers in terms of various aspects of their structure. There are potentially three contributions to the rotatory power: (*a*) that due to the (+)-1 : 3-dimethylbutyl groups, together with the groups to which they are immediately covalently bonded in the polymer, and that due to possible dissymmetry in (*b*) the primary, (*c*) the secondary, chain structure.

It is considered that the contribution of the asymmetric side groups, together with their immediate environment in the molecule, is substantially equal to the molecular rotation of (+)-1 : 3-dimethylbutyl pivalate, since the structures within the square brackets of (I) and (II) are identical. It is seen (Table 1) that the algebraic difference between the



molecular rotation of fully active poly[(+)-1 : 3-dimethylbutyl methacrylate] and that of the pivalate is a series of negative rotations of about one-third the magnitude of those of the pivalate. This rotatory power ($[M]_s$) is to be ascribed to structural features other than the individual ester units.

[8] Kendrew, Bodo, Dintzis, Parrish, Wyckoff, and Phillips, *Nature*, 1958, **181**, 662; Bernal, *Discuss. Faraday Soc.*, 1958, **25**, 7.

The present polymers all contain the polymethacryloyl main chain, the isotactic and the syndiotactic structure for which are represented by the Fischer projection formulæ (III) and (IV). As discussed earlier in relation to the literature, each of these structures has numerous " local " planes of symmetry, the first at every carbon atom, the second at every methylated carbon atom, whence it is inferred that neither configuration, nor random sequences of short sections of (III) and (IV) alternately, can give rise to optical activity, a conclusion supported by the experimental evidence.[1,9] Poly(methyl methacrylate) chains terminate largely by disproportionation at 60°,[10] and entirely so at 90°;[11] probably, therefore, the present polymethacrylates terminate by disproportionation and possess the symmetry associated with simple terminations.[1,2] It is concluded that the primary chain structure exhibits an overall symmetry, and therefore does not contribute to the rotatory power of the polymer.

Since a regular left- or right-hand helix is dissymmetric, the secondary structure can, in principle, contribute, and the rotations $[M]_s$ are ascribed to this source. Dissymmetric coiling of the main chain, conforming more to a right- than to a left-hand helix (or *vice versa*) may have arisen during polymerisation; alternatively it may be the most stable conformation of the chain molecule in solution, in each instance dissymmetric coiling being imposed by the steric requirements for the minimum-energy accommodation of the asymmetric side-groups.

Inspection of a C.R.L.-Catalin model of the syndiotactic polymer shows that the main chain conforms to a planar zig-zag only if the chain methyl groups and the carbonyl groups of the ester units are closely packed; a conformation providing maximum relaxation of packing requires rotation about links of the main chain such that the latter takes on a helical form, and since the conformation is to accommodate 1 : 3-dimethylbutyl groups which are asymmetric and all of the same configuration, a preference is to be expected for either a right- or a left-hand helix. For the isotactic configuration of the main chain, also, the closeness of packing renders a helical conformation probable.

From the stability of the rotatory power to change in molecular size, and in end groups, and to alteration in the larger-scale coiling associated with change in concentration, it is inferred that the secondary coiling, for a given temperature and solvent, is a stable, and, if averaged over more than a minimum number of units, a constant feature of the polymer chain.

The partially active polymers can be considered as copolymers of the optically pure (+)-methacrylate with the (±)methacrylate, and, with respect to these polymers, and the copolymers of the (+)-methacrylate and methyl methacrylate, it is of use to calculate the molecular secondary rotation due to units other than those of optically pure monomer. Evaluation of this quantity, $[M]_{sn}$, requires subtraction of a molecular-rotation component equivalent to the proportion of optically pure monomer present; it can be shown to be given by:

$$[M]_{sn} = m([\alpha] - [\alpha]'x)/100(1 - x)$$

where x is the weight-fraction of optically pure 1 : 3-dimethylbutyl methacrylate units present in the copolymer, $[\alpha]$ and $[\alpha]'$ are the specific rotation of the given polymer and of fully active poly[(+)-1 : 3-dimethylbutyl methacrylate], and m is the molecular weight of the second monomer. The assumption is made that, in its situation in the copolymer, the (+)-monomer unit contributes the same rotatory power as in the fully active (+)-polymer: that is, not only the component (*a*), above, but also that due to secondary coiling.

For the partially active polymer, the contribution, $[M]_{sn}$, from the (±)-units is found to be a series of small quantities of variable sign: it is inferred that these units are essentially optically inert, *d*-contributions of whatever kind being cancelled by the corresponding

[9] Beredjick and Schuerch, *J. Amer. Chem. Soc.*, 1958, **80**, 1933.
[10] Bevington, Melville, and Taylor, *J. Polymer Sci.*, 1954, **14**, 463.
[11] Bamford and Jenkins, *Nature*, 1955, **176**, 78.

XUM

l-contributions; the optically pure units contribute, proportionally, the same rotatory power as in the fully-active polymer.

With respect to the copolymers of fully active (+)-1 : 3-dimethylbutyl methacrylate with methyl methacrylate in molar ratio 1 : 2·33 and 1 : 3·20, the rotations deduced for the secondary structure of the methyl methacrylate units ($[M]_{sn}$, Table 1) are quantities of (+)-sign, opposite to that found for the secondary structure of the 1 : 3-dimethylbutyl methacrylate units. Further, the polymer richer in the latter possesses the larger values of $[M]_{sn}$. No explanation of the sign-difference is put forward; with respect to the difference in magnitude, it is possible that a left- rather than a right-hand helical form (or *vice versa*) of the methyl methacrylate sequences conforms better to adjacent (+)-1 : 3-dimethylbutyl methacrylate units, whence a greater proportion of the latter will increase the dissymmetry in coiling of the methyl methacrylate sequences, giving rise to a larger value of $[M]_{sn}$.

We thank the Department of Scientific and Industrial Research for a maintenance grant (to D. W. W.) and Imperial Chemical Industries Limited for participation in a grant.

BATTERSEA COLLEGE OF TECHNOLOGY, LONDON, S.W.11. [*Received, March 5th,* 1959.]

---

542. *Ipecacuanha Alkaloids. Part III.* The Stereochemistry at Positions 1′ and 10 of Emetine.*

By A. R. BATTERSBY, R. BINKS, and G. C. DAVIDSON.

Infrared evidence and conformational arguments are presented which strongly support conformation (VIII) as the thermodynamically most stable one for the benzoquinolizidine system (cf. VII).

The ester (VII; R = Me), prepared by degradation of *O*-methylpsychotrine, is shown to have an equatorial methoxyl group. It is established that no rearrangement occurs during preparation of this ester. The stereochemistry at positions 1′ and 10 in *O*-methylpsychotrine and emetine is thereby proved to be as in (XXII) and (XXIII), respectively.

OF the Ipecacuanha alkaloids,[1] particular interest attaches to emetine because of its importance in the treatment of amœbic dysentery. Its structure (I) was established by degradation [2] in 1949 and was confirmed by the synthesis of (±)-rubremetine [3] and of emetine itself,[4] but these studies gave no information about the stereochemistry of the alkaloid.

Our purpose in the present series of investigations is to elucidate the relative and absolute stereochemistry of emetine. It is clear that this knowledge will be of value in any explanation of the stereospecificity of emetine's pharmacological action and will also be of considerable interest in establishing the relation of emetine to other alkaloids, particularly those in the indole series, which are thought to have similar biogeneses.[5] Finally, work on the stereospecific synthesis of emetine requires first a knowledge of its stereochemistry.

Our degradative work which has been briefly described [6] in part, starts with *O*-methylpsychotrine (II). This occurs as a minor alkaloid in Ipecacuanha and a simple method for

* Part II, *J.*, 1959, 1748.

[1] Reviewed by Janot, "The Alkaloids," Ed. Manske and Holmes, Academic Press Inc., New York, 1953, Vol. III, p. 363.

[2] Pailer and Porschinski, *Monatsh.*, 1949, **80**, 94; Battersby and Openshaw, *J.*, 1949, 3207 and refs. therein.

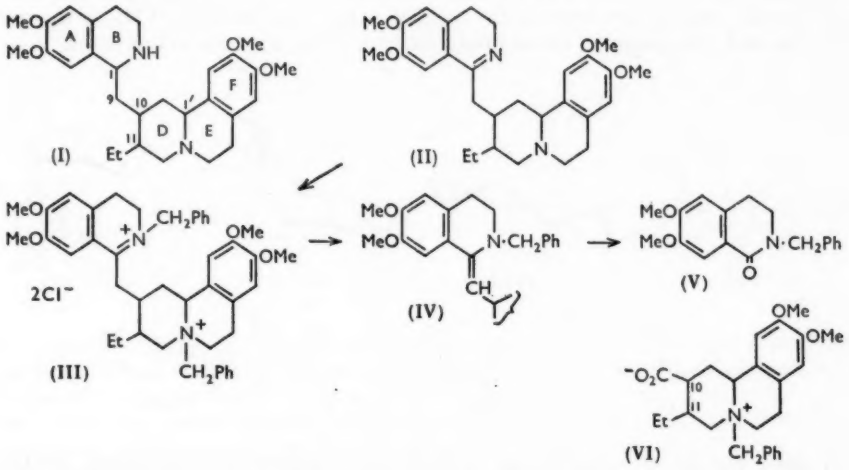
[3] Battersby and Openshaw, *Experientia*, 1950, **6**, 387; Battersby, Openshaw, and Wood, *J.*, 1953, 2463; Ban, *Pharm. Bull. (Japan)*, 1955, **3**, 53.

[4] Evstigneeva, Livshits, Bainova, Zakharkin, and Preobrazhenskii, *J. Gen. Chem.* (*U.R.S.S.*), 1952, **22**, 1467.

[5] Woodward, *Nature*, 1948, **162**, 155; Robinson, *ibid.*, p. 206; Woodward, *Angew. Chem.*, 1956, **68**, 13.

[6] Battersby, Binks, Davidson, Davidson, and Edwards, *Chem. and Ind.*, 1957, 982.

its isolation from that source is given on p. 2708. This alkaloid can be reduced chemically to a mixture of emetine and isoemetine; the latter differs from emetine [7] only in the configuration at position 1. We find that this reduction is more readily achieved by catalytic hydrogenation of *O*-methylpsychotrine base in ethanol.[8] These results prove that *O*-methylpsychotrine and emetine have the same stereochemistry about rings D and E; knowledge derived from one therefore holds for the other.



O-Methylpsychotrine with hot benzyl chloride yields the bisbenzylochloride (III) which in alkaline solution gave the iso-base (IV). This was very readily oxidised by potassium permanganate at −5° and, in addition to a water-soluble fraction, a crystalline neutral product, $C_{18}H_{19}O_3N$, was obtained in 53% yield. The latter was identical with our earlier preparation [9] of *N*-benzylcorydaline (V) and therefore the water-soluble product is presumably the quaternary betaine (VI). This was confirmed when hydrogenolysis of the crude betaine over palladium gave the crystalline amino-acid (VII; R = H) in 54% overall yield.

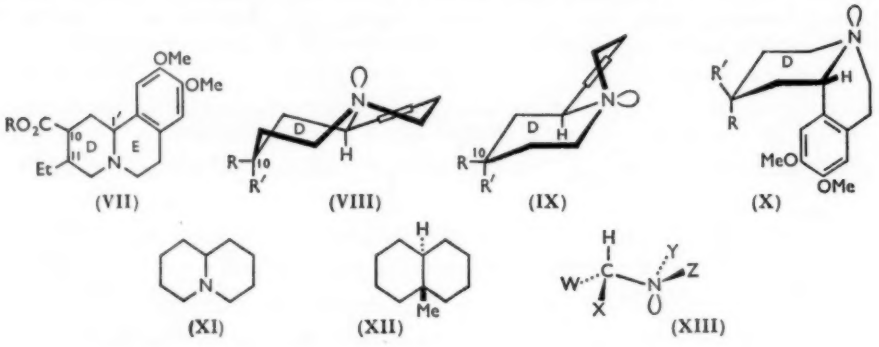
In order to study the configuration at $C_{(10)}$ in this amino-acid, the corresponding methyl ester (VII; R = Me) was heated with methanolic sodium methoxide under conditions selected to be considerably more vigorous than those which are known to invert the axial methoxycarbonyl group of ecgonine methyl ester.[10] Since our ester (VII; R = Me) was recovered unchanged, it follows that the methoxycarbonyl group is equatorial in the favoured conformation of the molecule.

If one makes in this case the safe restriction that only the chair and the half-chair form of rings D and E respectively should be considered, there are three possible conformations, (VIII), (IX), and (X) for the benzoquinolizidine system in the ester (VII; R = Me). As required of different conformations of a molecule, (VIII), (IX), and (X) are interconvertible owing to the ease with which the nitrogen atom can undergo inversion. Conformation (X) with the bulky aromatic group axial should clearly be the least stable. The *trans*-form (VIII) should be more stable than the corresponding *cis*-form (IX) because in the latter arrangement there are present [11] the skew interactions which make *cis*-decalin thermodynamically less stable than *trans*-decalin. It is worth noting, however, that comparisons

[7] Pyman, *J.*, 1917, **111**, 419.
[8] Cf. Karrer, Eugster, and Ruttner, *Helv. Chim. Acta*, 1948, **31**, 1219.
[9] Battersby and Davidson, unpublished work.
[10] Findlay, *J. Amer. Chem. Soc.*, 1954, **76**, 2855.
[11] Cf. Cookson, *Chem. and Ind.*, 1953, 337.

XUM

of stabilities of the possible conformations of quinolizidine (XI) with the thermodynamic stabilities of *cis*- and *trans*-decalin should consider the effect of the space requirement that the nitrogen electron pair exceeds that of a hydrogen atom.[12] This factor will act in favour of the *cis*-conformation (cf. IX), but it cannot outweight the forces which favour the *trans*-form (cf. VIII) because, though the bulk of a methyl group is accepted as greater than that of hydrogen or an electron pair,[12] *trans*-9-methyldecalin (XII) is thermodynamically more stable than the *cis*-isomer by 0·8 kcal. per mole.[13] Thus the foregoing consideration of non-bonded interactions leads to the conclusion that conformation (VIII) is the most stable one, and strong support comes from a study of infrared spectra in this series.



A large number of quinolizidine derivatives of known stereochemistry has been examined spectroscopically and it is found [14] that the infrared spectrum shows distinct absorption in the 2700—2800 cm.$^{-1}$ region only when the base contains at least two hydrogen atoms on the carbons attached to nitrogen arranged as in the system (XIII) with the C–H bond and the nitrogen electron pair *trans* and coplanar. This absorption also appears in the spectra of the indole alkaloids examined [15,16] which have an α-hydrogen atom at position 3 and *trans*-locked D, E rings. Again in these cases, the stereochemistry about the $C_{(3)}$–N system is unambiguously as in (XIII), when chair and half-chair rings are used, and two other hydrogen atoms are similarly orientated.

The many benzoquinolizidine bases (cf. VII) obtained in the present and subsequent work all show infrared absorption of medium intensity at 2750 ± 10 cm.$^{-1}$ which is not present in salts of the bases or in their 1′,*N*-unsaturated derivatives. Most of the spectra were determined with the base in solution or in the form of an amorphous film, so that the results are derived from molecules unconstrained by the intermolecular forces present in a crystal. Thus the favoured conformation of our benzoquinolizidine molecules must fulfil the stereochemical conditions described above for the reference compounds.* These requirements are met only by conformation (VIII) which can now be accepted confidently as the preferred one.

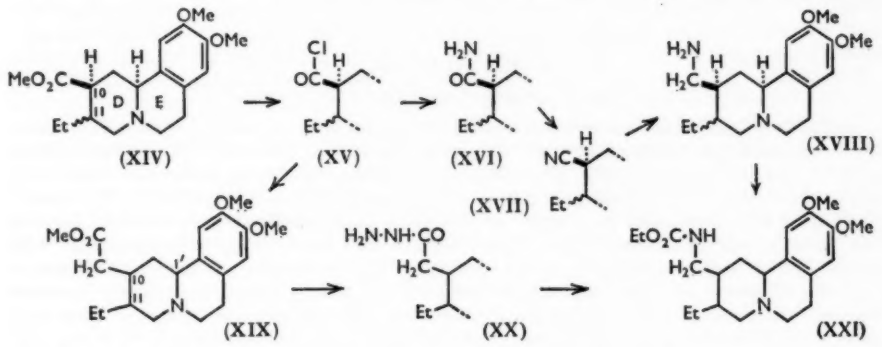
It follows that the ester (VII; R = Me), having an equatorial methoxycarbonyl group, must be represented by (VIII; R = CO_2Me, R′ = H) which in a planar representation

* It has recently been shown [17] that *N*-methyl groups give rise to an absorption band close to the one discussed above and presumably of similar origin. Confident assignment of an absorption in this region might therefore be difficult in some alkaloids. Our bases do not contain *N*-methyl groups, so this problem does not arise.

[12] Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44 and refs. therein.
[13] Turner, *J. Amer. Chem. Soc.*, 1952, **74**, 2118.
[14] Bohlmann, *Angew. Chem.*, 1957, **69**, 641; *Chem. Ber.*, 1958, **91**, 2157.
[15] Wenkert and Roychaudhuri, *J. Amer. Chem. Soc.*, 1956, **78**, 6417.
[16] Neuss and Boaz, *J. Org. Chem.*, 1957, **22**, 1001.
[17] Hill and Meakins, *J.*, 1958, 760; Braunholtz, Ebsworth, Mann, and Sheppard, *J.*, 1958, 2780.

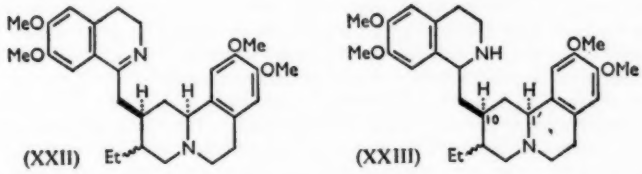
becomes (XIV); the ***absolute*** configuration shown has been selected for reasons presented elsewhere.[18]

Since the ester (XIV) has the more stable configuration at position 10, it is necessary to prove that inversion has not occurred during its preparation and isolation. This problem was studied as shown in the annexed scheme. The sodium salt derived from the ester



(XIV) reacted with oxalyl chloride to afford the acid chloride (XV). When this was subjected to Arndt–Eistert homologation, a reaction which is known to proceed with retention of configuration,[19] the ester (XIX) (below) was obtained. This result is in favour of the same stereochemistry for the two esters (XIV) and (XIX), but it was not considered to be fully satisfactory because of the low yield of the ester (XIX). A longer sequence of reactions gave the required conclusive proof.

The acid chloride (XV) with ammonia gave the amide (XVI) which was dehydrated by hot phosphoryl chloride to the nitrile (XVII). When the nitrile was reduced with lithium aluminium hydride, the amine (XVIII) was obtained and this, without purification, was converted by ethyl chloroformate into the urethane (XXI). The same urethane resulted from Curtius rearrangement of the hydrazide (XX) prepared from the ester (XIX) and which, in turn, was derived from protoemetine.[20] None of these transformations has affected any of the asymmetric centres and therefore it follows that the ester (XIV) and (XIX) have the same stereochemistry about rings D and E. Further, we proved earlier [20] that the ester (XIX) has the same stereochemistry as *O*-methylpsychotrine. Thus, this also holds for the ester (XIV) and it is established that no inversion has occurred in the reaction sequence used for its preparation. The stereochemistry shown in (XIV) can be used therefore to extend the structures of *O*-methylpysychotrine and emetine to (XXII) and (XXIII), respectively.



Recently, Brossi *et al.*[21] with Barash and Osbond [22] have interpreted the results obtained in the synthesis of the isomers of emetine, together with related experiments, on the basis

[18] Battersby and Garratt, *Proc. Chem. Soc.*, 1959, 86.
[19] Wiberg and Hutton, *J. Amer. Chem. Soc.*, 1956, **78**, 1640.
[20] Battersby and Harper, *J.*, 1959, 1748.
[21] Brossi, Cohen, Osbond, Plattner, Schnider, and Wickens, *Chem. and Ind.*, 1958, 491.
[22] Barash and Osbond, *ibid.*, p. 490.

XUM

of a stereochemistry for emetine having the opposite *relative* configuration at position 1′ to that shown in structure (XXIII), that is a *trans*-arrangement of the 1′- and the 10-hydrogen atom. This proposal is in conflict with our experiments [23] and Dr. Osbond has since very kindly sent to us, in advance of publication, a communication [24] describing new pharmacological tests on their synthetic emetine isomers. The results obtained are now in agreement with the stereochemistry shown in structure (XXIII).

Experimental

For general directions, see Part I of this series.[25]

Isolation of O-*Methylpsychotrine* (II).—The crude bases (60 g.) recovered [25] from the mother-liquors obtained in the extraction of emetine, were dissolved in warm ethanol (400 ml.) containing hydrated oxalic acid (40 g.). The precipitated hydrogen oxalates were collected from the warm solution and then heated to the b. p. with ethanol (150 ml.). A mixture of *O*-methylpsychotrine and emetamine hydrogen oxalates (20·5 g.) crystallised from the cold solution. This mixture was distributed between ethyl acetate (250 ml.) and aqueous phosphate buffer (500 ml.) made from 0·5M-KH_2PO_4 (5 vol.) and 0·5M-K_2HPO_4 (3 vol.). The separated aqueous layer was shaken again with ethyl acetate (50 ml.), and the combined organic solutions were extracted with fresh buffer (4 × 250 ml.). After the combined aqueous layers had been made strongly alkaline, the precipitated base was extracted into ether–chloroform (5 : 1 by vol.; 4 × 250 ml.). Evaporation of the dried extracts left a gum (18 g.) which was dissolved in dry ether, and the solution was filtered. The filtrate was concentrated to a thin syrup; *O*-methylpsychotrine crystallised (12 g.; m. p. 121—123°). Brindley and Pyman [26] record m. p. 123—124° (corr.).

Crude emetamine was obtained by evaporation of the above combined solutions in ethyl acetate.

O-*Methylpsychotrine Bisbenzylochloride* (III).—A solution of *O*-methylpyschotrine (5 g.) in freshly distilled benzyl chloride (30 ml.) was heated at 80° for 12 hr. Half of the benzyl chloride was then evaporated at 0·1 mm. and the residual solution was poured into dry ether (300 ml.). The precipitated solid *salt* was powdered under the ether, washed several times with ether by decantation, and then dried at 100° *in vacuo* (7·28 g., 96%) (Found: C, 70·8; H, 7·3; N, 3·6. $C_{43}H_{52}O_4N_2Cl_2$ requires C, 70·6; H, 7·2; N, 3·8%).

Oxidation of O-*Methylpsychotrine Bisbenzylochloride*.—A stirred solution of the bisbenzylochloride (6 g.) in rigorously purified dioxan (100 ml.) and water (100 ml.) at 0° was treated with 2N-sodium hydroxide (10 ml.). The solution was then cooled to −5° and aqueous potassium permanganate (150 ml. containing 3 g.) was added dropwise under the surface during 45 min. with stirring. After filtration of the resultant suspension and washing of the pad with warm dilute sodium hydroxide and acetone, the filtrate was adjusted to pH 2 with concentrated hydrochloric acid (*A*).

Five similar oxidations of the bisbenzylochloride (total 33 g.) were carried out and the solutions from the six runs were combined at stage (*A*) above. The organic solvents were evaporated and the aqueous suspension was extracted thrice with ethyl acetate; the aqueous layer was reserved (*B*). After the ethyl acetate solution had been washed with dilute hydrochloric acid and water, it was dried and evaporated to leave a gum which was extracted with hot ether. Concentration of the extract afforded *N*-benzylcorydaline (V) as needles (7·22 g., 53%), m. p. 96—99° undepressed on admixture with an authentic sample.[9]

The aqueous solution (*B*) was extracted with chloroform (3 × 100 ml.), the combined chloroform solutions were shaken with 0·5N-sodium hydroxide (3 × 100 ml.), and the alkaline extracts were acidified and added to the main aqueous solution. This was evaporated to dryness, and the residue was dried for 1 day over phosphoric oxide *in vacuo* and then extracted with boiling ethanol until the insoluble material contained nothing organic. Water (20 ml.) and hydrated sodium acetate (10 g.) were added to the combined extracts (400 ml.) which were then shaken with 10% palladised charcoal (2 g.) and hydrogen at room temperature and pressure. Uptake

[23] Battersby, *Chem. and Ind.*, 1958, 1324.
[24] Osbond, *ibid.*, 1959, 257.
[25] Battersby, Davidson, and Harper, *J.*, 1959, 1744.
[26] Brindley and Pyman, *J.*, 1927, **130**, 1067.

of gas (1·4 l.) ceased after 15 hr. and the solution was then filtered. Evaporation of the filtrate left a gum which was dissolved in dilute hydrochloric acid, and the solution was basified. This was extracted thrice with ethyl acetate, and the aqueous layer was acidified to Congo Red and then evaporated to dryness. After the residue had been dried over phosphoric oxide *in vacuo* for 1 day, it was extracted with several portions of boiling ethanol to dissolve all the organic material. Evaporation of the extracts left a gum which was heated under reflux for 5 hr. with methanol (500 ml.) and concentrated sulphuric acid (20 ml.). Methanol (400 ml.) was distilled off and the solution was poured on ice and aqueous sodium carbonate. Ether-extraction of the resultant alkaline suspension gave, by the usual working up, a gum (9·29 g.) which was extracted (2 × 200 ml.) with hot light petroleum (b. p. 40—60°). The insoluble residue was dissolved in ether (5 ml.), and light petroleum (150 ml.) was added to precipitate an amorphous solid (0·36 g.) which was rejected. The three solutions in light petroleum were combined and extracted with 2N-hydrochloric acid (3 × 100 ml.) to give an acidic aqueous solution (*C*) which was heated under reflux for 14 hr. and then evaporated to 75 ml. Addition of concentrated hydrochloric acid (7 ml.) caused separation of the *amino-acid hydrochloride* (cf. VII; R = H) as prisms (6·6 g.), m. p. 264—266° (decomp.), unchanged by recrystallisation from a mixture of concentrated hydrochloric acid (1 vol.) and water (3 vol.). Concentration of the original mother liquor gave more of the same salt (total yield, 9·03 g., 54%). The amino-acid hydrochloride also separated as fine needles from a rapidly cooled solution, but on being kept in contact with the mother-liquor these changed into compact prisms (Found: C, 61·0; H, 7·3; N, 3·8. $C_{18}H_{26}O_4NCl$ requires C, 60·75; H, 7·4; N, 3·9%), $[\alpha]_D^{20}$ −46·5° ± 1° (*c* 3·1 in water).

In a similar degradation of *O*-methylpsychotrine (10 g.), solution (*C*) above was made alkaline with potassium carbonate, and the crude amino-ester (VII; R = Me) was extracted with ether. Evaporation of the ether left a gum (3·6 g.) which was distilled in a short-path still at 150° (bath)/0·2 mm. The distillate (2·9 g.) was heated under reflux with 0·2N-barium hydroxide (75 ml.) for 7½ hr. and the cooled solution was treated with exactly one equiv. of 0·5N-sulphuric acid. After the barium sulphate had been filtered off, the solution was evaporated to dryness to leave the *amino-acid* (VII; R = H) as prisms which, crystallised from ethanol or from water (1·5 g.), had m. p. 193—200° (decomp.), strongly dependent on the rate of heating; a slow temperature rise gave m. p. 185—194° (Found, in material dried at 110°: C, 63·4; H, 8·0; N, 3·7. $C_{18}H_{25}O_4N,H_2O$ requires C, 64·1; H, 8·1; N, 4·1%).

The Amino-ester (VII; R = Me).—A solution of the foregoing amino-acid hydrochloride (1 g.) in methanol (50 ml.) containing concentrated sulphuric acid (2 ml.) was heated under reflux for 12 hr. Part of the methanol (40 ml.) was then distilled off and the solution was poured on ice and sodium carbonate. Ether-extraction then afforded the *amino-ester* (VII; R = Me) as a gum (0·9 g., 97%) which crystallised from light petroleum (b. p. 40—60°) as rosettes of needles, m. p. 73·5—75·5° (Found, in material dried at 56°: C, 68·9; H, 8·2; N, 4·4. $C_{19}H_{27}O_4N$ requires C, 68·5; H, 8·2; N, 4·2%).

Action of Sodium Methoxide on the Amino-ester (VII; R = Me).—A solution of the above ester (0·11 g.) in methanolic sodium methoxide (2 ml.), made by dissolving sodium (0·29 g.) in methanol (51 ml.), was heated under reflux for 11 hr. 2N-Hydrochloric acid (0·3 ml.) was then added, the solution was evaporated to dryness, and the residue was heated under reflux with 2N-hydrochloric acid (10 ml.) for 24 hr. This solution was then evaporated to dryness and the residue was dried in *vacuo* for 24 hr. before it was dissolved quantitatively in a mixture (5 ml.) of ethanol (3 vol.) and water (1 vol.) for the determination of rotation. $[\alpha]_D^{20}$ was −45·5° ± 1° calculated as amino-acid hydrochloride (cf. VII; R = H). Concentration of the solution yielded the unchanged amino-acid hydrochloride (cf. VII; R = H) (0·08 g.), m. p. and mixed m. p. 264—266° (decomp.), $[\alpha]_D^{19}$ −45° ± 1°.

A second sample (0·11 g.) of the amino-ester (VII; R = Me) was handled as above, but the treatment with sodium methoxide was omitted. $[\alpha]_D^{20}$ of the final solution was −43·4° ± 1° calculated as above.

Arndt–Eistert Homologation.—The foregoing amino-acid hydrochloride (534 mg., 1·5 mmol.), which had been dried at 100° over phosphoric oxide *in vacuo* for 7 hr., was dissolved in water (10 ml.) and treated with 0·5N-sodium hydroxide (6 ml.). Evaporation of the solution to dryness left a crystalline residue which was powdered in an agate mortar and dried at 100° over phosphoric oxide in *vacuo* for 1·5 hr. This mixture of salts (517 mg.) was stirred at room temperature in dry benzene (30 ml.) while freshly distilled oxalyl chloride (0·169 ml.) in benzene (2·5 ml.) was added during 5 min.; the oxalyl chloride was then washed in with more benzene

(5 ml.). After the suspension had been stirred for 0·5 hr., most of the solid had dissolved and the last traces were removed by filtration through a filter stick in an apparatus completely protected against moisture. The resultant clear solution was added to an ethereal solution of diazomethane (*ca.* 0·7 g.), kept overnight at room temperature, and evaporated to dryness at 10°, to leave the diazo-ketone as a gum (286 mg.).

Silver oxide, freshly prepared from silver nitrate (0·25 g.), was washed many times with water, methanol, and finally with anhydrous methanol. The product was added to a solution of the above diazo-ketone in anhydrous methanol (10 ml.) at 50°; nitrogen evolution (26 ml.) was complete in 2 hr. After the solution had been filtered, it was evaporated to dryness and the residue was dissolved in ether (2 ml.) containing a few drops of methanol to give a clear solution. This was mixed with light petroleum (50 ml.), b. p. 40—60°, then kept until the petroleum solution was clear, and the solution was decanted; the same procedure was repeated twice on the petroleum-insoluble matter. The combined extracts were shaken with 0·2N-hydrochloric acid (2 × 15 ml.), the aqueous solution was extracted with ether (3 × 50 ml.), then basified with potassium carbonate and extracted again with ether (3 × 50 ml.). Evaporation of the latter ethereal solution gave a gum (122 mg.) which was extracted thoroughly with boiling light petroleum (b. p. 40—60°); the combined extracts were concentrated to 2 ml., crystallisation occurring to give needles, m. p. 93—94°, depressed to 58—65° on admixture with the methyl ester (VII; R = Me).

The crystalline ester and the gum obtained by evaporation of its mother-liquor were hydrolysed separately by boiling 2N-hydrochloric acid (5 ml.). Concentration of both solutions (to 0·5 ml.) yielded crystals of the homologated amino-acid hydrochloride (46·3 mg., 15 mg. respectively; 11%), and both crops when dried at room temperature had m. p. and mixed m. p. 179—183°, after sintering at 176°. After a sample of the former crop had been dried at 40° for 3 hr., the m. p. was 199—202°, after slight sintering.

Part (24·3 mg.) of the combined crops of hydrochloride above was converted as earlier into the methyl ester (23·5 mg.) which crystallised from light petroleum (b. p. 40—60°) to give the amino-ester (XIX), m. p. 93—94° undepressed on admixture with an authentic sample.[20] The two samples of (XIX) gave identical *X*-ray powder diagrams.

Preparation of the Amide (XVI).—A benzene solution of the amino-acid chloride (XV) was prepared as above, though without filtration, on the 1 mmol. scale. An excess of dry ammonia was passed through the solution, and the benzene was evaporated to leave a solid which was dissolved in 0·2N-hydrochloric acid (8 ml.). The acidic solution was filtered and basified with ammonia, to precipitate a solid (239 mg.), m. p. 239—240°, which was collected and washed with water. Recrystallisation once from aqueous ethanol, containing 30% of ethanol, gave the *amide* (XVI) as prisms, m. p. 243—244° (decomp.) (Found: C, 68·2; H, 8·4. $C_{18}H_{26}O_3N_2$ requires C, 67·9; H, 8·2%).

The Benzoquinolizidine Nitrile (XVII).—The foregoing amide (146 mg.) was heated for 35 min. with freshly distilled phosphorus oxychloride (1·2 ml.) in a bath at 112—123°. Ice (10 g.) was then added to the cooled solution and, when the decomposition of the phosphorus oxychloride was complete, the solution was made strongly alkaline with sodium carbonate. The precipitated solid was collected, washed with water, and dried (136 mg.; m. p. 157—158°). Recrystallisation from aqueous ethanol, containing 30% of ethanol, afforded the *nitrile* (XVII) as fine needles, m. p. 158—159° (Found: C, 71·9; H, 8·3; N, 9·4. $C_{18}H_{24}O_2N_2$ requires C, 72·0; H, 8·1; N, 9·3%).

Preparation of the Hydrazide (XX).—A mixture of the methyl ester[20] (XIX) (0·1 g.) and anhydrous hydrazine (0·5 ml.) was heated on the steam-bath, and anhydrous methanol (15 drops) was added to give a clear solution. This was heated on the steam-bath for 24 hr., then cooled, and the crystals were collected, washed with water, and dried [82 mg.; m. p. 206—207° (decomp.)]. The m. p. of the *hydrazide* was unchanged by recrystallisation from ethanol (Found: C, 65·2; H, 8·5. $C_{19}H_{28}O_3N_3$ requires C, 65·6; H, 8·4%).

Preparation of the Ethyl Urethane (XXI).—(a) *From the foregoing hydrazide.* A solution of dry hydrogen chloride (7·3 mg.) in anhydrous ethanol (0·35 ml.) was added to a suspension of the above hydrazide (34·6 mg.) in anhydrous ethanol (1 ml.). The resultant clear solution was treated at 0° during 2 min. with pentyl nitrite (13·8 mg.) in ethanol (1·01 ml.). After the mixture had warmed to room temperature, it was kept for 1 hr. and then heated under reflux for 24 hr. The solution was concentrated to 0·5 ml., made alkaline with ammonia, and treated with water until turbid. Crystals (34·1 mg.), m. p. 138—140°, separated and were recrystallised

from aqueous ethanol, to give the *ethyl urethane* (XXI) as needles, m. p. 139·5—140·5° (Found: C, 67·4; H, 8·6. $C_{21}H_{32}O_4N_2$ requires C, 67·0; H, 8·6%).

(b) *From the nitrile* (XVII). The nitrile was dried at 78° for 3 hr. over phosphoric oxide in *vacuo* and then added as a solution in anhydrous ether (20 ml.) during 5 min. to a suspension of lithium aluminium hydride (0·1 g.) in ether (10 ml.). After the mixture had been heated under reflux for 1·5 hr., it was cooled and treated with water (0·15 ml.), then with 20% aqueous sodium hydroxide (0·1 ml.), and finally with water (0·5 ml.). The granular precipitate was filtered off and washed with much hot ether. Evaporation of the dried ethereal solution left a gum (99 mg.). This was dissolved in dry purified dioxan (2·5 ml.) and treated at room temperature with triethylamine (0·08 ml.) in dioxan (0·5 ml.), followed by ethyl chloroformate (0·12 ml.) in dioxan (0·12 ml.). The mixture was heated at 50—55° for 30 min., then diluted with water (3 ml.) and freed from dioxan by evaporation. Basification of the resultant solution with ammonia precipitated a solid (88 mg.), m. p. 135—137°, raised to 138·5—139·5° by recrystallisation from aqueous ethanol. The m. p. was unchanged on admixture with the urethane (XXI) from (*a*) above and the two samples of urethane had identical infrared spectra (Nujol).

Grateful acknowledgment is made to Dr. H. T. Openshaw and the Wellcome Foundation Limited, and to Mr. H. E. Glynn and Messrs. Whiffen and Sons, Limited, for generous supplies of Ipecacuanha residues, to the Chemical Society for a grant from the Research Fund, and to the Department of Scientific and Industrial Research for a Maintenance Award (to R. B.).

THE UNIVERSITY, BRISTOL. [*Received, March 16th*, 1959.]

---

543. *Autoxidation of Hindered Phenols in Alkaline Media. Part I.*

By H. R. GERSMANN and A. F. BICKEL.

The autoxidation of substituted 2,6-di-t-butylphenols in alkaline media has been studied at various temperatures. 2,4,6-Tri-t-butylphenol and 4-methyl-2,6-di-t-butylphenol are oxidized to hydroperoxycyclohexadienones, the structures of which have been established. The formation of hydroperoxides appeared to be autocatalytic, the catalyst probably being a decomposition product of a 2,4,6-trialkyl-2-hydroperoxycyclohexa-3,5-dienone. Oxidation may also be catalyzed by quinones and aromatic polynitrocompounds, and these reactions were most suited to kinetic studies. Mechanisms for these reactions are put forward. 2,6-Di-t-butylphenol is oxidized to the corresponding diphenoquinone and a by-product, $C_{13}H_{22}O_3$.

THE oxidation of hindered phenols has been extensively studied during the last few years, *e.g.*, with benzoyl peroxide,[1] bromine,[2] alkaline ferricyanide,[3,4] lead dioxide,[4] and hydroperoxides.[5] The behaviour of these phenols as inhibitors of free-radical oxidation has been studied also in this laboratory.[6] More recently the autoxidation of 2,6-di-t-butylphenols in an alkaline medium was investigated by Kharasch,[7] Ley,[8] and the present authors,[9] and Weissberger[10] studied the alkaline autoxidation of substituted quinols. In this paper a detailed account is given of the alkaline autoxidation of 2,6-di-t-butylphenol, 2,4,6-tri-t-butylphenol, and 4-methyl-2,6-di-t-butylphenol (cf. ref. 9).

[1] Cosgrove and Waters, *J.*, 1949, 3189.
[2] Coppinger and Campbell, *J. Amer. Chem. Soc.*, 1951, **75**, 734.
[3] Müller and Ley, *Chem. Ber.*, 1954, **87**, 922.
[4] Cook, Nash, and Flanagan, *J. Amer. Chem. Soc.*, 1955, **77**, 1783.
[5] Campbell and Coppinger, *ibid.*, 1952, **74**, 1469.
[6] Bickel and Kooyman, *J.*, 1953, 3211; 1956, 2215; 1957, 2217, 2415.
[7] Kharasch and Yoshi, *J. Org. Chem.*, 1957, **22**, 1439.
[8] Ley, *Angew. Chem.*, 1958, **70**, 74.
[9] Bickel and Gersmann, *Proc. Chem. Soc.*, 1957, 231.
[10] Luvalle and Weissberger, *J. Amer. Chem. Soc.*, 1947, **69**, 1567.

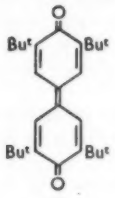
XUM

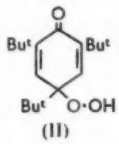
Results

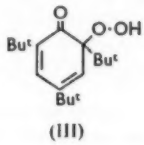
Oxidation Products.—Autoxidations were effected by vigorous stirring of a solution of the phenol and excess of potassium hydroxide in 90% ethanol with gaseous oxygen at 40°. After absorption of 1 mol. of oxygen, products were isolated by ether-extraction of the acidified mixture and subsequent crystallization.

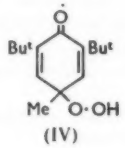
In this way 2,6-di-t-butylphenol yielded 3,3′,5,5′-tetra-t-butyldiphenoquinone (I) (~50%) and a compound, $C_{13}H_{22}O_3$ (~25%). 2,4,6-Tri-t-butylphenol yielded 4-hydroperoxy-2,4,6-tri-t-butylcyclohexa-2,5-dienone (II) and 2-hydroperoxy-2,4,6-tri-t-butylcyclohexa-3,5-dienone (III) (total about 75%).

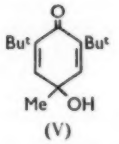
4-Methyl-2,6-di-t-butylphenol gave as the main product 4-hydroperoxy-4-methyl-2,6-di-t-butylcyclohexa-2,5-dienone (IV).

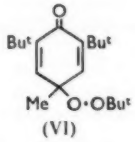

(I)

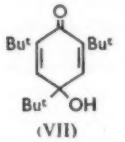

(II)


(III)


(IV)


(V)


(VI)


(VII)

The structure of the hydroperoxide (IV) was established in the following manner. The presence of one atom of active oxygen was shown by a peroxide determination. The isolated reduction product (V) and the hydroperoxide have ultraviolet absorption spectra very similar to that of the peroxide (VI), which was described by Bickel and Kooyman.[6] This peroxide was obtained from both the hydroperoxide (IV) and the alcohol (V) by reaction with t-butyl alcohol and t-butyl hydroperoxide, respectively, in 70% sulphuric acid. The structure of the hydroperoxides (I) and (III) was primarily based upon determinations of carbon, hydrogen, and active oxygen and was further established by the close resemblance between the ultraviolet absorption spectra of compounds (II) and (IV) and of (III) and the "*ortho*"-peroxides isolated by Bickel and Kooyman.[6]

The new hydroperoxides (II), (III), and (IV) have interesting properties: The first two can be partially transformed into each other: after the hydroperoxide (II) had been heated for 2 hours at 40° (pH 14) in alcohol in the presence of oxygen, ultraviolet spectroscopic analysis revealed the presence of 19·5% of the isomer (III) and 30·5% of the original compound (V) (ratio 39/61). Under the same conditions, the isomer (III) was partly converted into (II) (ratio found: 42/58). Ultraviolet absorption spectra also point to this type of isomerization in the case of the analogue (IV).

Secondly, the isomerizations are accompanied by partial decomposition, which was studied by allowing the peroxide (IV) to decompose in ethanol at 40° (pH 14) in the presence of oxygen or nitrogen. With oxygen about 80% of the hydroperoxide had decomposed after 4 hours; ultraviolet absorption spectra showed that the main reaction product was the alcohol (V). In the absence of oxygen, 90% of the hydroperoxide had decomposed after 2 hours, and ultraviolet analysis revealed that the product was a 2 : 3-mixture of the alcohol (V) and 4-methyl-2,6-di-t-butylphenol.

Finally, it was found that reduction of the peroxides (II) and (IV) with hydrogen iodide gave the corresponding alcohols (VII) and (V). It was not possible to isolate a similar product on reduction of the peroxide (III).

Kinetics of the Oxidation.—(a) *General survey of rate measurements.* Oxidation of 4-methyl-2,6-di-t-butyl- and of 2,4,6-tri-t-butyl-phenol was studied at various temperatures and pressures. The rates of oxygen uptake were determined by measuring a change in volume at atmospheric pressure or a change in pressure at lower oxygen pressures (see Experimental section). Stirring was always so fast that it could be assumed that the solution was saturated with oxygen. In nearly all experiments the yield of hydroperoxides was between 70% and 85%. Light metals

XUM

and ions of heavy metals slightly enhanced the rate of oxidation, so the measurements were made in the dark and in the presence of potassium cyanide as a complex-forming agent. However, potassium cyanide also accelerated the decomposition of the quinone catalyst (see below) and was therefore omitted in the study of the catalyzed reactions. Table 1 lists the maximum rates of oxygen uptake and the hydroperoxide yields in a number of autoxidations with different starting conditions.

(b) *Determination of the dissociation constants of the phenols.* To correlate rates of oxidation with the ionization of the phenols, the dissociation constants were determined in 90% ethanol by ultraviolet spectroscopy: 2,4,6-tri-t-butyl-, pK 14·0 ± 0·2; 4-methyl-2,6-di-t-butyl-, pK 13·7 ± 0·2; and 2,6-di-t-butyl-phenol, pK 13·6 ± 0·2. The pH dependence of the oxidation rate for the catalyzed (see below) and for the uncatalyzed reaction is illustrated in Tables 1 and 2.

(c) *Autocatalysis.* As the form of the oxidation curves pointed to autocatalysis, the hydroperoxides as well as some other possible products were tested for catalytic activity. It was found that the *ortho*-hydroperoxide (III) is responsible for the catalytic effect (cf. the experimental curves reproduced in Fig. 1), and there are indications that this peroxide decomposes to give small amounts of the actual catalyst. This assumption was made as the rates found with added " *ortho* "-hydroperoxide decreased soon after the beginning of each run (the run being started by adding a mixture of phenol and catalyst dissolved in ethanol to a solution of potassium hydroxide). When, however, the phenol dissolved in ethanol was added to a potassium

TABLE 1. *Maximum rates (ml./min.) and yields (%) of hydroperoxide in autoxidation of phenols in 90% ethanol.*

Temp.	pH	Phenol (mmole)	Solvent (ml.)	Rate	Yield	Temp.	pH	Phenol (mmole)	Solvent (ml.)	Rate	Yield
		2,6-*Di-t-butyl*-4-*methylphenol*						2,4,6-*Tri-t-butylphenol*			
−10°	14	1	28	0·04		0°	14	1	—	0·04	
0	13	1	28	~0·01		25	14·15	1	28	0·65	66
25	14	1	28	1·65	95	25	14	1	28	0·65	81
40	12	1	28	0·08	55	25	14	0·6	28	0·28	84
40	13	1	28	0·80	75	25	13·7	1	—	0·3	
40	14	5	28	54		40	13	1	28	0·70	60
40	14	2	56	14·4		40	14	1	28	2·65	63
40	14	1	28	6·9		60	14	1	—	12	40
40	13	2	56	1·60	77						
40	13	2	28	1·80	71						
60	12	1	28	~0·40	38						
60	13	1	28	3·60	45						

TABLE 2. *First-order rate constants (k in mole/min.) of catalyzed oxidation of 4-methyl-2,6-di-t-butylphenol (1 mmole).*

Catalyst (mg.)	O_2 (cm.)	Temp.	pH	k *	Catalyst (mg.)	O_2 (cm.)	Temp.	pH	k *
	2,6-*Di-t-butylbenzoquinone*						*Duroquinone*		
20	76	−10°	14	0·172	20	76	0°	13	0·0531
100	76	−10	14	0·175	100	76	0	13	0·0680
50	15·2	−10	14	0·0379					
1	76	0	13	0·049			m-*Dinitrobenzene*		
5	76	0	13	0·0634	20	76	−10	14	0·0046
10	76	0	13	0·0672	50	76	−10	14	0·0104
20	76	0	13	0·0670	50	15·2	−10	14	0·060
100	76	0	13	0·0668	100	76	0	13	0·00745
50	76	0	13	0·0660	25	76	0	13	0·00243
50	51	0	13	0·0398	50	76	0	14	0·0192
50	37	0	13	0·0295	50	52	0	14	0·0161
50	19	0	13	0·0184	50	34	0	14	0·0170
20	76	0	14	0·392	50	17	0	14	0·0102
100	76	0	14	0·398	20	76	0	14	0·0088
22	76	40	14	5·5			ortho-*Hydroperoxide* (I)		
2,6-*Di-t-butylbenzoquinone*, 20 *mg.*, + *duroquinone*, 20 *mg.*					9·7	76	40	13	0·17
					10	76	25	13	0·039
—	76	0°	13	0·0667	20	76	25	13	0·057
					40	76	25	13	0·076

* Concn. calc. from O_2 consumption.

XUM

hydroxide solution of the catalyst the slower rate was observed from the start. Hence it appears that some decomposition product of the peroxide, possibly an *ortho*-quinone or a radical, is the active catalyst. This catalyst then would be more stable in ethanol than in potassium hydroxide, thus causing the effects found at the start of the rate measurements.

Since ultraviolet absorption spectroscopy points to the formation of a small amount of an *ortho*-hydroperoxide from 4-methyl-2,6-di-t-butylphenol, the same type of autocatalysis is assumed in this case.

The *para*-hydroperoxide (IV) is inactive as a catalyst.

(d) *Other catalysts.* During the search for the autocatalyst in the oxidation of 4-methyl-2,6-di-t-butylphenol other catalysts were discovered. When these are added at the start of the reaction simpler kinetics are obtained and consequently a large number of these catalyzed reactions have been studied. 2,6-Di-t-butylbenzoquinone, duroquinone, and *m*-dinitrobenzene proved extremely useful. The reactions were generally of the first order (calculated from oxygen uptake) with respect to phenol concentration. First-order rate constants are listed in Table 2.

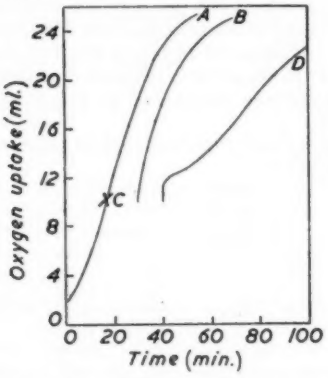


FIG. 1. *Autocatalysis in the oxidation of* 2,4,6-*tri-t-butylphenol.*

A, Phenol alone (1 *mmole*).
B, Phenol mixed with ortho-*hydroperoxide* (I) *as analysed at the point C.*
D, The amount of phenol analysed at point C.

(e) *Experiments on the reaction mechanism.* It was shown that the addition of a hydrogen donor (9,10-dihydroanthracene), free radicals (2,4,6-tri-t-butylphenoxyl), or free-radical-producing substance (2,2′-azoisobutyronitrile) had no definite effect on the oxidation rate.

DISCUSSION

Mechanism of the Oxidation of 2,4,6-*tri-t-butyl- and* 4-*methyl*-2,6,-*di-t-butylphenol.*— A first plausible assumption about the mechanism of the autoxidation of hindered phenols seemed to be that of a free-radical chain process very commonly encountered in autoxidations. However, the various tests which we made to find evidence for a free-radical chain mechanism, and the nature of the active catalysts (quinones and aromatic polynitro-compounds), which are inhibitors in radical reactions, indicated that the idea was incorrect. The kinetics of the catalyzed autoxidations enable a formal description of the reactions to be given.

(a) pH-*dependence.* From the results (Table 2) and the dissociation constants of the phenols it is concluded that the phenoxide ion is the reactive species.

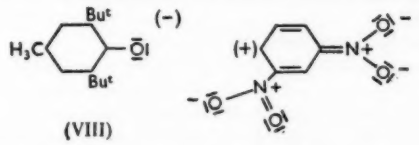
(b) *Catalysis by* m-*dinitrobenzene.* The rate is of the first order in phenol, dependent on catalyst concentration and independent of oxygen pressure between 0·5 and 1 atm. (reactions 1 and 2):

$$R^- + \text{Catalyst} \rightleftharpoons (R, \text{catalyst})^- \quad \ldots\ldots\ldots\ldots (1)$$

$$(R, \text{catalyst})^- + O_2 \longrightarrow RO_2^- + \text{Catalyst} \quad \ldots\ldots\ldots\ldots (2)$$

We have here a case of normal catalysis in which the catalyst and the substrate form a reactive intermediate. This intermediate is tentatively considered to be an electron donor–acceptor complex for which a structure (VIII) may represent one of the resonance hybrids. It is possible that in this way the phenol part of the molecule has a temporary

free-radical character, permitting rapid reaction with oxygen. The interaction between phenol and catalyst has still to be proved, however. Some experiments have also been



(VIII)

carried out with 1,3,5-trinitrobenzene. Catalysis of the same order of magnitude as with *m*-dinitrobenzene was found, but the catalyst decomposes rapidly. Nitrobenzene is inactive.

Catalysis by quinones. Quinones were the most active catalysts. As with the nitro-compounds, the quinones partially decompose during the autoxidation. With 2,6-di-t-butylquinone the rate is independent of catalyst concentration (from 5% onward) and proportional to the oxygen pressure. Although this phenomenon, called saturation of catalysis, is also known in oxidation of quinol, an explanation similar to that given by Luvalle and Weissberger [10] is very improbable in the autoxidation of monohydric phenols.* At present it is preferable to explain the experimental results formally by equations 3 and 4:

$$R^- + O_2 \rightleftharpoons (R^-,O_2) \quad \ldots \quad (3)$$

$$(R^-,O_2) + \text{Catalyst} \xrightarrow[\text{fast}]{} RO_2^- + \text{Catalyst} \quad \ldots \quad (4)$$

It is not yet possible to prove such an interaction with oxygen prior to the actual oxidation step in this system owing to the decomposition of the catalyst mentioned earlier.

The kinetics obtained with duroquinone catalyst are in agreement with the scheme given for 2,6-di-t-butylbenzoquinone. The rate constant is somewhat lower and there is some dependence on the catalyst concentration, indicating that reaction (4) is contributing to the rate-determining step. In accordance with expectation, the rate observed with a mixture of duroquinone and 2,6-di-t-butylbenzoquinone is equal to the rate found with the latter alone.

(d) *Properties of the hydroperoxides.* The isomerization and decomposition of the hydroperoxides are considered to be a sequel to the autoxidation of the phenols, resulting, among other things, in the formation of the active catalyst mentioned above.

(e) *Oxidation of 2,6-di-t-butylphenol.* The formation of 3,3',5,5'-tetra-t-butyldiphenoquinone on autoxidation of 2,6-di-t-butylphenol might indicate that a radical chain mechanism is more likely in this case. Indeed, the rate of oxidation of a mixture of this phenol and the antioxidant 4-methyl-2,6-di-t-butylphenol is smaller than the sum of the components.

The kinetics of oxidation when the peroxide (III) is used as a catalyst are rather involved. The Arrhenius energies of activation found for the various reactions are given in Table 3.

TABLE 3. *Energies of activation of alkaline oxidation of 4-methyl-2,6-di-t-butylphenol.*

Catalyst	E (cal./mole)	log A (min.$^{-1}$)
2,6-Di-t-butylbenzoquinone	12,000	9·25
m-Dinitrobenzene (20 mg./mmole)	8900	5·43
m-Dinitrobenzene (50 mg./mmole)	9400	5·49
Nil	20,000	

EXPERIMENTAL

With W. ROEST and (MISS) J. VERHEY.

Starting Materials.—2,4,6-Tri-t-butylphenol, obtained by alkylation of phenol with t-butyl alcohol and sulphuric acid at 70°, had m. p. 130°.

* They assume interaction between the semiquinone radical-ion and quinone. As no free phenoxy-radicals can be detected in phenol autoxidation, we assume that the complex between phenol and quinone exists until after the oxidation, thus rendering an interaction with another quinone molecule unlikely.

4-Methyl-2,6-di-t-butylphenol (II) of technical quality was recrystallized several times from methanol and light petroleum ether (b. p. 60—80°); it then had m. p. 71·0°.

2,6-Di-t-butylphenol, obtained by alkylation of phenol with t-butyl alcohol and aluminium phenoxide, had m. p. 38°.

Ethanol was purified by Pestemer's procedure.[11]

Preparation and Decomposition of Hydroperoxides.—*4-Hydroperoxy-4-methyl-2,6-di-t-butylcyclohexa-2,5-dienone* (IV). A solution of 4-methyl-2,6-di-t-butylphenol (1 mmole) in a N-solution (25 ml.) of potassium hydroxide in 90% ethanol absorbed 1 mmole of oxygen in 5 min. at 40°. The mixture was then acidified and the products were extracted with ether. After recrystallization from light petroleum (b. p. 60—80°) the *hydroperoxide* was obtained (75% yield) with m. p. 115° (Found: C, 71·1; H, 9·6%; *M*, 274. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·6%; *M*, 253). Hydroperoxide analysis by Tobolsky and Mesrobian's method [12] showed the presence of one atom of active oxygen per molecule (equiv., 127). The product obtained after reduction is the alcohol (V), m. p. 113° (Found: C, 75·9; H, 10·5. Calc. for $C_{15}H_{24}O_2$: C, 76·2; H, 10·2%).

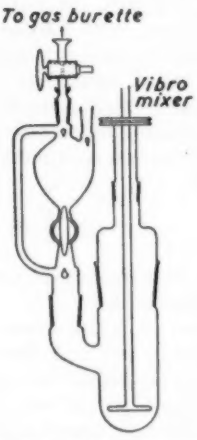


FIG. 2. *Oxidation vessel with Vibro mixer.*

Hydroperoxides from Tri-t-butylphenol.—Reaction with oxygen as described above also yielded 75% of peroxidic material. After preparation of about 20 g. of this material it was possible to obtain the hydroperoxides (II) and (III) (Found, for both compounds: C, 73·8; H, 10·5. Calc. for $C_{18}H_{30}O_3$: C, 73·5; H, 10·2%) by careful fractional crystallization from nitroethane and mesityl oxide with continuous checking by ultraviolet spectroscopy.

The alcohol (VII) obtained on reduction of the peroxide (II) had m. p. 126—130°.

Ultraviolet Absorption Spectra.—These were generally measured for iso-octane solutions with a Cary recording spectrophotometer Model 14 M.L.S.-50.

Kinetic Measurements.—Most of the kinetic measurements were carried out in the apparatus shown in Fig. 2. This apparatus was connected to a gas-burette in which the quantity of oxygen consumed was measured. Measurements at constant volume were carried out in a completely closed system in which differences in pressure were read with a cathetometer. By using a relatively large gas volume the total difference in pressure was always kept below 20 mm. In this way the reaction took place at practically constant total pressure, while the accurate cathetometer readings were used to measure the reaction velocity. Results are shown in Tables 1 and 2. For the reactions without added catalyst the maximum velocity is given. The reactions where a catalyst was added at the start of the reaction were often of first order in phenol concentration, and this constant is given. In other cases the oxygen uptake during the first two minutes is quoted. The reaction mixture was generally analyzed by titration and ultraviolet spectroscopy. The method for calculating the rate constant must be carefully selected, since two possible errors may be introduced when only the oxygen consumption is determined. In the first place, there is a volume effect when the phenol and hydroxide solutions are mixed. This is probably due to the finite time necessary for mixing. We assume that the oxygen consumed during this time has indeed reacted. In the second place, side reactions which consume or liberate oxygen contribute to the calculated phenol consumption. We tried to avoid these errors by using Guggenheim's method for the calculation of first-order rate constants. The results were, however, unsatisfactory, probably because this method attaches relatively more weight to the later stages of the reaction just when side reactions become more important. Calculation of the rate constant based on the actual volume of oxygen taken up during the reaction proved to be the best method.

KONINKLIJKE/SHELL-LABORATORIUM, AMSTERDAM
(N.V. DE BATAAFSCHE PETROLEUM MAATSCHAPPIJ).

[*Received, April 21st*, 1958.
Revised, February 25th, 1959.]

[11] Pestemer, *Angew. Chem.*, 1951, **63**, 118.
[12] Tobolsky and Mesrobian, "Organic Peroxides," Interscience Publ. Inc., New York, 1954.

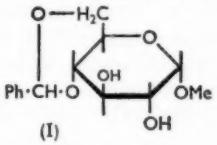
XUM

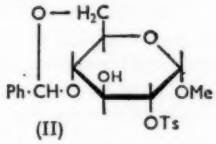
544. *The* O-*Toluene*-p-*sulphonyl Derivatives of* 1,5-*Anhydro*-4,6-O-*benzylidene*-D-*glucitol.**

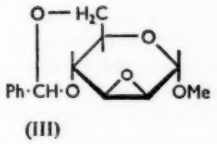
By F. H. Newth.

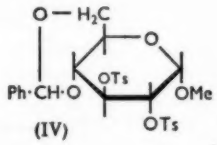
It has been shown that selective acylation of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol occurs at position 2, and that the epoxide produced from the 2,3-di-*O*-toluene-*p*-sulphonyl derivative has the *allo*-configuration. This is parallel to the reactions of the corresponding derivatives of methyl α-D-glucoside and it is concluded, therefore, that in this case the glycosidic methoxyl group does not exert any profound directing influence.

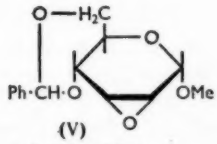
In the well-established sequence for the conversion of methyl 4,6-*O*-benzylidene-α-D-glucoside (I) into the corresponding derivative of D-altrose (VI) by alkaline hydrolysis of either the *manno*-epoxide [1] (III) or the *allo*-epoxide [2] (V) there are two features which have not received attention. The first is the selective formation of the 2-toluene-*p*-sulphonyl ester (II) and the second is the alkaline hydrolysis of the 2,3-ditoluene-*p*-sulphonyl ester (IV). Careful experimental work by Richtmyer and Hudson has shown that only methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-alloside (V) and no methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside (III) is formed.

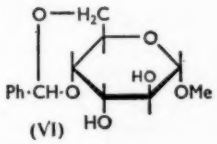

(I)


(II)


(III)


(IV)

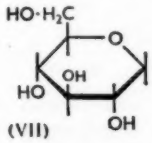

(V)

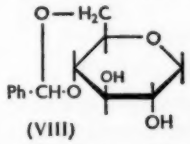

(VI)

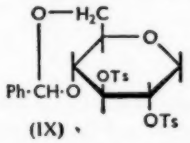
(Ts = *p*-$C_6H_4Me\cdot SO_2$)

The equivalent reactions of the *O*-toluene-*p*-sulphonyl derivatives of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol have now been investigated to see whether the origin of these orientations lies in the glycosidic methoxyl group. Its influence could be either steric because of its axial disposition or electronic by virtue of its being part of the acetal system and thus able to induce positive character at $C_{(1)}$.

In continuing their study of the 1,5-anhydrohexitols, Zissis and Richtmyer [3] have prepared 1,5-anhydro-D-altritol from 1,5-anhydro-D-glucitol (poligalitol) (VII). The


(VII)


(VIII)


(IX)

constitution of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol (VIII) was established by periodate oxidation and the epoxide obtained by alkaline hydrolysis of the 2,3-ditoluene-*p*-sulphonate (IX) could have had either the *manno*- (X) or the *allo*-configuration (XI). By

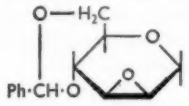
* An abstract of this paper was presented at the XVIth Internat. Congr. of Pure Appl. Chem., Paris, 1957.

[1] Robertson and Griffith, *J.*, 1935, 1193.
[2] Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1727.
[3] Zissis and Richtmyer, *ibid.*, 1955, **77**, 5154.

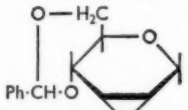
XUM

analogy with the reactions in the glucoside series, it was denoted as 1,5:2,3-dianhydro-4,6-*O*-benzylidene-D-allitol (XI). Alkaline hydrolysis of the epoxide led predominantly to 1,5-anhydro-4,6-*O*-benzylidene-D-altritol (XII), the axial isomer, in conformity with the Fürst and Plattner rule [4] whichever the configuration.

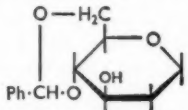
It has now been shown that Zissis and Richtmyer's assumption of epoxide configuration was correct and, further, that 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol (VIII) is selectively acylated at position 2 as is the corresponding derivative of methyl α-D-glucoside.



(X)

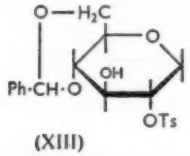


(XI)

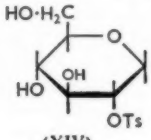


(XII)

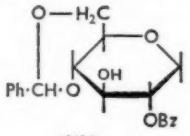
The restrained reaction of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol with toluene-*p*-sulphonyl chloride (1 mol.) in pyridine yielded a monotoluene-*p*-sulphonate which was identical with that which accompanies the formation of the 2,3-di-toluene-*p*-sulphonate.[3] This was shown to be 1,5-anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (XIII) by the fact that the 1,5-anhydro-*O*-tosyl-D-glucitol (XIV), obtained by acidic hydrolysis of the benzylidene residue, consumed 1 mol. of periodate. Monobenzoylation of the diol (VIII) gave 1,5-anhydro-2-*O*-benzoyl-4,6-*O*-benzylidene-D-glucitol (XV). The structure of this follows from the difference between its *O*-toluene-*p*-sulphonyl derivative (XVI) and 1,5-anhydro 3-*O*-benzoyl-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (XVII) obtained from (XIII). Both sulphonic and carboxylic esterification have occurred at position 2 and the conformational formulæ (Ia) and (VIIIa) show that it cannot be the glycosidic methoxyl group which is solely responsible for this orientation. It is not at present apparent why the 2-hydroxyl group should react rather than that at position 3 which is also equatorial.



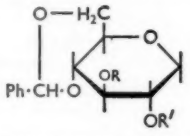
(XIII)



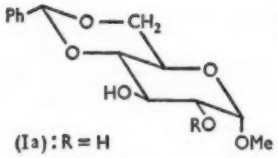
(XIV)



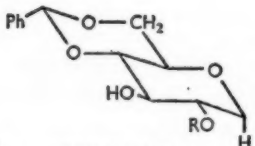
(XV)



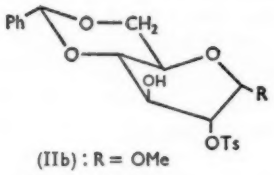
(XVI): R = Ts, R' = Bz
(XVII): R = Bz, R' = Ts



(Ia): R = H
(IIa): R = Ts



(VIIIa): R = H
(XIIIa): R = Ts



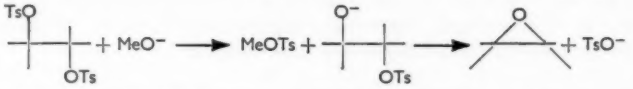
(IIb): R = OMe
(XIIIb): R = H

1,5-Anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (XIII) was treated with sodium methoxide at 0° and was smoothly converted into an epoxide which must be 1,5:2,3-dianhydro-4,6-*O*-benzylidene-D-mannitol (X). It is interesting to compare the ease of this reaction with the more severe conditions which are required to hydrolyse the corresponding methyl α-D-glucoside [1] (II). It has been suggested [5] that in a diequatorial system, such as that which is present here, there must be a conformational shift to the boat form (IIb) and (XIIIb) when both groups are axial and suitably placed for intramolecular nucleophilic displacement. To attain this diaxial state, the *cis*-groups at positions 1 and 2 in (IIa) and

[4] Mills, cited by Newth and Homer, *J.*, 1953, 989.
[5] Newth, *J.*, 1956, 441.

(XIIIa) must move past each other and will show interaction appropriate to their size. The different reactivities shown by (II) and (XIII) are attributed to the different passing interactions: OTs/OMe and OTs/H.

1,5:2,3-Dianhydro-4,6-*O*-benzylidene-D-mannitol (X) was compared with the dianhydride obtained by Zissis and Richtmyer from 1,5-anhydro-4,6-*O*-benzylidene-2,3-di-*O*-tosyl-D-glucitol (IX): the two compounds were clearly different. The 2,3-ditoluene-*p*-sulphonate must give the allitol (XI) and this is parallel to the behaviour of methyl 4,6-*O*-benzylidene-2,3-di-*O*-tosyl-α-D-glucoside (IV). The factors controlling epoxide formation from di-*O*-sulphonyl compounds are little known, but a preliminary appraisal has been given recently.[6] Angyal and Gilham [7] represent the reaction by the sequence:



and the more accessible sulphonyl group is that which is removed first. In the diesters (IV) and (IX) primary attack must be at the 2-group and although the reason for this is not yet apparent, it cannot be attributed to the presence or absence of the glycosidic methoxyl group.

Experimental

1,5-*Anhydro*-4,6-O-*benzylidene*-D-*glucitol*.—The compound, m. p. 165—166°, was prepared as described by Zissis and Richtmyer [3] (Found: C, 61·9; H, 6·4. Calc. for $C_{13}H_{16}O_5$: C, 61·9; H, 6·4%).

1,5-*Anhydro*-4,6-O-*benzylidene*-2-O-*tosyl*-D-*glucitol*.—1,5-Anhydro-4,6-*O*-benzylidene-D-glucitol (252 mg.) was dissolved in dry pyridine (2 ml.) and cooled to −10°. Toluene-*p*-sulphonyl chloride (190 mg., 1 mol.) was added and the mixture kept at 5° for 48 hr. The crystalline material obtained on pouring the solution into water recrystallised from ethanol, and 1,5-*anhydro*-4,6-O-*benzylidene*-2-O-*tosyl*-D-*glucitol* (260 mg.) had m. p. 174—175° (alone or mixed with 1,5-anhydro-4,6-*O*-benzylidene-*O*-tosyl-D-glucitol, m. p. 175—179°, kindly supplied by Dr. N. K. Richtmyer) (Found: C, 58·9; H, 5·6. $C_{20}H_{22}O_7S$ requires C, 59·1; H, 5·4%).

1,5-*Anhydro*-2-O-*tosyl*-D-*glucitol*.—1,5-Anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (200 mg.) was boiled in methanol (5 ml.) containing 3N-hydrochloric acid (0·5 ml.) for 20 min., then kept for 18 hr. Water (5 ml.) was added, the acid neutralised with silver carbonate, and benzaldehyde extracted with ether. The inorganic material was removed at a centrifuge and evaporation of the solution provided crystalline 1,5-*anhydro*-2-O-*tosyl*-D-*glucitol* (125 mg.). Recrystallised from ethyl acetate, it had m. p. 158—159° (Found: C, 49·1; H, 5·6. $C_{13}H_{18}O_7S$ requires C, 49·1; H, 5·6%): it reduced 1·02 mol. of sodium metaperiodate during 49 hr.

1,5-*Anhydro*-2-O-*benzoyl*-4,6-O-*benzylidene*-D-*glucitol*.—1,5-Anhydro-4,6-*O*-benzylidene-D-glucitol (252 mg.) in pyridine (2 ml.) was treated at −10° with benzoyl chloride (0·116 ml.) and kept at 0° for 3 hr., then poured into water, giving a crystalline precipitate which separated into two fractions when recrystallised from ethanol. The first was 1,5-*anhydro*-2,3-*di*-O-*benzoyl*-4,6-O-*benzylidene*-D-*glucitol* (85 mg.), m. p. 162—163° (Found: C, 70·7; H, 5·5. $C_{27}H_{24}O_7$ requires C, 70·5; H, 5·2%). The second was 1,5-*anhydro*-2-O-*benzoyl*-4,6-O-*benzylidene*-D-*glucitol* (60 mg.), m. p. 133—134° (Found: C, 67·8; H, 5·7. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6%).

1,5-*Anhydro*-2-O-*benzoyl*-4,6-O-*benzylidene*-3-O-*tosyl*-D-*glucitol*.—1,5-Anhydro-2-*O*-benzoyl-4,6-*O*-benzylidene-D-glucitol (25 mg.) in pyridine (0·1 ml.) was treated with toluene-*p*-sulphonyl chloride (20 mg.) for 4 hr. The mixture was poured into water; 1,5-*anhydro*-2-O-*benzoyl*-4,6-O-*benzylidene*-3-O-*tosyl*-D-*glucitol*, recrystallised from ethanol, had m. p. 192° (Found: C, 63·3; H, 5·2. $C_{27}H_{26}O_8S$ requires C, 63·5; H, 5·1%).

1,5-*Anhydro*-3-O-*benzoyl*-4,6-O-*benzylidene*-2-O-*tosyl*-D-*glucitol*.—1,5-Anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (50 mg.) in pyridine (0·5 ml.) was treated with benzoyl chloride (0·05 ml.) for 3 hr. The mixture was poured into water; 1,5-*anhydro*-3-O-*benzoyl*-4,6-O-*benzylidene*-2-O-*tosyl*-D-*glucitol*, recrystallised from ethanol, had m. p. 200° (m. p. in admixture

[6] Newth, *Quart. Rev.*, 1959, **13**, 30.
[7] Angyal and Gilham, *J.*, 1957, 3691.

with the above isomer: 170—185°) (Found: C, 63·3; H, 5·1%). The infrared spectra of the two compounds showed differences in the region of molecular absorption (9—15 μ), the 2-*O*-benzoyl-3-*O*-tosyl derivative having bands displaced to longer wavelength and with different relative intensity.

1,5:2,3-*Dianhydro*-4,6-O-*benzylidene*-D-*mannitol*.—1,5-Anhydro-4,6-*O*-benzylidene-2-*O*-tosyl-D-glucitol (60 mg.) in chloroform (0·3 ml.) was treated with methanol (0·3 ml.) containing sodium (10 mg.) and kept at 0° for 14 hr. The alkali was neutralised with carbon dioxide, the solution evaporated, and the residue extracted with chloroform. Evaporation of the extract gave crystalline 1,5:2,3-*dianhydro*-4,6-O-*benzylidene*-D-*mannitol* (25 mg.). Recrystallised from ethanol this had m. p. 138—139°, $[\alpha]_D^{22}$ −13·2° (*c* 0·85 in chloroform) (Found: C, 66·5; H, 5·9. $C_{13}H_{14}O_4$ requires C, 66·6; H, 6·0%). In admixture with the 1,5:2,3-dianhydro-4,6-*O*-benzylidene-D-hexitol, m. p. 129—130°, $[\alpha]_D^{20}$ +35°, of Zissis and Richtmyer[3] (kindly supplied by Dr. N. K. Richtmyer), there was a depression to 95—103°. That compound must, therefore, be 1,5:2,3-dianhydro-4,6-*O*-benzylidene-D-allitol.

This work was carried out during the tenure of an I.C.I. Fellowship in the University of Cambridge. The author gratefully acknowledges a generous gift of 1,5-anhydro-D-glucitol from Dr. N. K. Richtmyer and thanks the Directors of " Shell " Research Ltd. for providing the opportunity to present this work at the XVIth International Congress of Pure and Applied Chemistry.

CARRINGTON RESEARCH LABORATORY, PETROCHEMICALS LTD.,
URMSTON, MANCHESTER. [*Received, February 9th*, 1959].

---

545. *The Synthesis and Isomeric Rearrangement of* 1-*Phenylallyl Chloride.*

By G. VALKANAS and E. S. WAIGHT.

1-Phenylallyl chloride has been prepared by the reaction of 1-phenylallyl alcohol and thionyl chloride either in ether in the presence of tri-n-butylamine or in chloroform in the presence of triethylamine. It rearranges rapidly and quantitatively to *trans*-cinnamyl chloride, and this reaction, which also accompanies its solvolyses, has been investigated kinetically in various solvents. The rearrangement is of the first order and its rate is related to parameters measuring the ionizing power of the medium, but not to the dielectric constant. It is concluded that in aqueous dioxan the formation of an intimate ion-pair is rate-determining, but that in other media an S_Ni' mechanism may be involved. The rate is increased by the addition of salts and of carboxylic acids, and the increase is proportional to the concentration of lithium chloride in ethanol and in *NN*-dimethylformamide, and to the concentration of acid in chlorobenzene.

WHEREAS migration of double bonds accompanying nucleophilic substitution in allylic halides has been much investigated,[1] the isomeric rearrangements of the halides themselves have been studied only for interconversions of 1- and 3-methylallyl chloride[2] and bromide,[3] 1,1- and 3,3-dimethylallyl chloride,[4] and *cis*- and *trans*-5-methylcyclohex-2-enyl chloride.[5] The low anionotropic mobility of such halides and the difficulty of obtaining quantitative rate data led us to turn to the phenylallyl chlorides, particularly since the anionotropy of phenylallyl alcohols[6] and esters[7] has been extensively studied. One of the required isomers, 3-phenylallyl (cinnamyl) chloride (II), is well known but the

[1] De Wolfe and Young, *Chem. Rev.*, 1956, **56**, 753.
[2] Kharasch, Kritchevsky, and Mayo, *J. Org. Chem.*, 1937, **2**, 489.
[3] England, *J.*, 1955, 1615; England and Hughes, *Nature*, 1951, **168**, 1002.
[4] Young, Winstein, and Goering, *J. Amer. Chem. Soc.*, 1951, **73**, 1958.
[5] Goering, Nevitt, and Silversmith, *ibid.*, 1955, **77**, 5026.
[6] Braude, Jones, and Stern, *J.*, 1946, 396.
[7] Braude, Turner, and Waight, *J.*, 1958, 2396; Braude and Turner, *J.*, 1958, 2404.

preparation of the other, 1-phenylallyl chloride (I), proved difficult although ultimately very simply achieved.

Synthesis.—Since the equilibrium in the system:

$$\text{(I) Ph·CHCl·CH:CH}_2 \rightleftharpoons \text{Ph·CH:CH·CH}_2\text{Cl (II)}$$

should very largely favour the conjugated isomer, the preparation of (I) can only succeed under non-equilibrating conditions. After unsuccessful attempts by other routes,[8] direct replacement of the hydroxyl group in 1-phenylallyl alcohol was investigated. The disadvantage of this lies in the known sensitivity of the alcohol and the suspected sensitivity of the product to the acidic reagents required. Cinnamyl chloride proved, indeed, to be the only isolable product from the reactions of 1-phenylallyl alcohol with phosphorus trichloride, phosphorus pentachloride, or thionyl chloride in ether, even in the presence of pyridine or triethylamine.* Following the discussion of the reaction of thionyl chloride with allylic alcohols given by Young, Caserio, and Brandon,[9] we tried the reaction of 1-phenylallyl alcohol with thionyl chloride in ether in the presence of tri-n-butylamine, whose hydrochloride is ether-soluble. A mixture of phenylallyl chlorides containing a high proportion of the 1-phenyl isomer was obtained. A much more convenient procedure was the treatment of the alcohol with thionyl chloride and triethylamine in dry chloroform, a good solvent for triethylamine hydrochloride. 1-Phenylallyl chloride is probably formed by bimolecular (S_N2) attack of chloride ion on the intermediate chlorosulphinate, but the latter also rearranges intramolecularly (S_Ni') to cinnamyl chloride. Rapid fractionation of the product under reduced pressure gave a chloride which had the correct elemental composition for (I) and exhibited strong infrared bands characteristic of a vinyl group (983 and 930 cm.$^{-1}$), but which also showed a weaker band at 965 cm.$^{-1}$ indicative of *trans* −CH=CH− in cinnamyl chloride. The presence of the latter was confirmed by the ultraviolet absorption ($\lambda_{max.}$ 2530 Å, ε 3500). The spectral data indicate that the product consists of 1-phenylallyl and cinnamyl chlorides in the ratio of about 5 : 1. The presence of some cinnamyl chloride, which could not readily be removed, did not in the main prove objectionable, and for brevity the mixture will be referred to as 1-phenylallyl chloride.

Rearrangement.—1-Phenylallyl chloride can be kept unchanged for some weeks under anhydrous conditions at −196°, or for shorter periods in ether solution at room temperature. At room temperature the undiluted chloride isomerizes rapidly and quantitatively to *trans*-cinnamyl chloride, identified by its ultraviolet and infrared absorption spectra. This isomerization, in conjunction with the analytical data, establishes the structure of the chloride as (I). Hydrolysis yields mainly 1-phenylallyl alcohol together with a little cinnamyl alcohol, and is accompanied by a competitive rearrangement to cinnamyl chloride, which is hydrolysed much more slowly to a mixture of the same alcohols but in different proportion.[10]

The very marked contrast in stability between the chloride itself and its solutions, and the variations observed from preparation to preparation, suggest that the apparently spontaneous isomerization may in fact be partly catalysed by traces of impurities. One of the most likely catalysts is hydrogen chloride, either from the preparation or more probably produced by interaction of 1-phenylallyl chloride with traces of water.

Initial kinetic studies of the rearrangement were made in chlorobenzene, the increase in intensity of the 2530 Å absorption band of cinnamyl chloride being used to follow the reaction. The rearrangement is of the first order, the product being essentially pure *trans*-cinnamyl chloride as in the absence of solvent. The rate constants (k) are reasonably

* Martin and Trinh (*Compt. rend.*, 1949, **228**, 688) claim to have isolated 1-phenylallyl chloride in 2% yield from the reaction of either 1-phenylallyl alcohol or cinnamyl alcohol with dry hydrogen chloride. We have been unable to repeat their preparation.

[8] Cf. Braude and Waight, *J.*, 1952, 1116.
[9] Young, Caserio, and Brandon, *Science*, 1953, **117**, 473.
[10] Valkanas and Waight, *Proc. Chem. Soc.*, 1959, 8.

XUM

reproducible for runs with samples from a particular preparation but vary quite widely with samples from different preparations.

Isomerization accompanies all solvolyses of 1-phenylallyl chloride so far investigated, so that rate data for a range of solvents of widely differing dielectric constants and ionizing powers are available (Table 1). In most of the solvents used the rate constants are far

TABLE 1. *Rearrangement of* 1-*phenylallyl chloride*, 40°. *The effect of medium.*

Medium	10^4k (min.$^{-1}$)	D^{20}	Z	E (kcal. mole^{-1})
Chlorobenzene	~0·28 *	5·9	55·8 †	~22
2-Nitropropane	~0·28 *	25	—	—
Dimethylformamide	3·4 *	36·7	68·5	19
2-Methylbutan-2-ol	20·4	12	70·4 †	—
Propan-2-ol	206	26	76·3	—
Ethanol	632	25·7	79·6	16
85% Dioxan–water	740	8	79·2	16
Methanol	~3800 *	34	83·6	—

* Estimated.
† Unpublished measurements by J. Crossley.

more reproducible than in chlorobenzene, but otherwise the kinetic features are identical in all solvents. For comparison, k's are referred to a temperature of 40°; where no direct measurements were made at this temperature, values have been estimated by

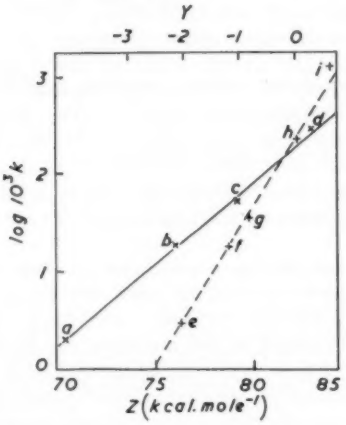


FIG. 1.

a 2-Methylbutan-2-ol at 40°.
b Propan-2-ol at 40°.
c Ethanol at 40°.
d Methanol at 40°.
e 90% Dioxan–water at 25°.
f 85% ,, ,,
g 80% ,, ,,
h 70% ,, ,,
i 60% ,, ,,

extrapolation of the Arrhenius curve. There is obviously no parallel between k and the dielectric constant of the medium (D) but log k is directly related to parameters measuring the ionizing power of the solvent, such as Grunwald and Winstein's Y values[11] and Kosower's Z values,[12] as shown in Fig. 1. Straight lines of different slope are obtained for a series of alcohols, and for various mixtures of dioxan and water. The values for chlorobenzene and *NN*-dimethylformamide lie below the extrapolation of the alcohol plot but give a line of similar slope. Z is the energy of the charge-transfer transition of 1-ethyl-4-methoxycarbonylpyridinium iodide in the solvent, and its use as a measure of solvent-ionizing power has been criticized by Winstein and Robinson.[13] However, Y, which is derived from the rate of solvolysis of t-butyl chloride in the medium, cannot be determined for all solvents, so that the use of Z is appropriate in the present instance. In the Grunwald–Winstein relation, log $k = mY +$ constant, m provides a measure of the susceptibility of the system to the ionizing power of the medium, referred to t-butyl

[11] Grunwald and Winstein, *J. Amer. Chem. Soc.*, 1948, **70**, 846.
[12] Kosower, *J. Amer. Chem. Soc.*, 1958, **80**, 3253.
[13] Winstein and Robinson, *J. Amer. Chem. Soc.*, 1958, **80**, 169.

chloride in aqueous ethanol as unity. m is large for reactions occurring by the S_N1 mechanism, for example the solvolyses of t-butyl halides, and low for reactions occurring by the S_N2 (or S_Ni) mechanism. For the isomeric rearrangement of 1-phenylallyl chloride in aqueous dioxan, m is 1·0, but in the alcoholic solvents m, derived from the plot of log k against Z, is only 0·5.

The energy of activation, E_A, also varies with the medium, paralleling the rate variation. Values of E_A derived from Table 2 are 22 kcal. mole^{-1} in chlorobenzene, 19 kcal. mole^{-1} in dimethylformamide, and 16 kcal. mole^{-1} in 85% dioxan.

TABLE 2. *Rearrangement of* 1-*phenylallyl chloride. The effect of temperature.*

(a) *In chlorobenzene containing* p-*nitrobenzoic acid.* (*Chloride concn.* 0·177 *mole l.*$^{-1}$, *acid concn.* 0·024 *mole l.*$^{-1}$.)

Temp.	90°	100°	110°	120°
10^4k (min.$^{-1}$)	59	132	255	590

(b) *In dimethylformamide.* (*Chloride concn.* 0·15 *mole l.*$^{-1}$.)

Temp.	61°	70°	80°	90°
10^4k (min.$^{-1}$)	22·3	45·5	103	217

(c) *In* 85% *dioxan–water.* (*Chloride concn.* 0·159 *mole l.*$^{-1}$.)

Temp.	25°	30°	35°	40°
10^4k (min.$^{-1}$)	213·5	319	514	740

TABLE 3. *Rearrangement of* 1-*phenylallyl chloride in chlorobenzene,* 90°. (*Chloride concn.* 0·30 *mole l.*$^{-1}$.) *The effect of acid.*

Acid	None	Monochloro-acetic	Dichloro-acetic	Trichloro-acetic	Trichloro-acetic	Trichloro-acetic	Trichloro-acetic
Concn. (mole l.$^{-1}$) ...	—	0·010	0·010	0·004	0·006	0·008	0·010
10^4k (min.$^{-1}$)	40	146	230	160	250	280	360

Braude [14] suggested that the isomeric rearrangement of allyl chlorides should exhibit acid-catalysis * and accordingly we have investigated the effect of various carboxylic acids in chlorobenzene. The rate of rearrangement is in fact increased by the addition of acid and the increase is proportional to the acid concentration and related to the strength of the acid, as shown in Table 3. Cinnamyl esters could not be detected in the reaction products although they are stable in chlorobenzene in the presence of hydrogen chloride at 90°. The energy of activation is decreased by the addition of acid. In the presence of 0·024M-*p*-nitrobenzoic acid, which has little effect on the rate, E_A is 22 kcal. mole^{-1}, and this value is probably not very different from that of the uncatalysed reaction in chlorobenzene. In the presence of trichloroacetic acid E_A is much lower, about 15 kcal. mole^{-1}. In comparison, E_A for 1-phenylallyl *p*-nitrobenzoate in chlorobenzene is about 26 kcal. mole^{-1},[7] and the difference of 4 kcal. mole^{-1} accounts almost entirely for the much lower mobility, about one-thousandth, in the ester compared with the chloride, since the non-exponential factors are similar for the two derivatives.

The effect of adding lithium chloride has also been examined. In both dimethylformamide and ethanol the increase in the rate of rearrangement is directly proportional to the salt concentration up to 0·5M in dimethylformamide and 1·0M in ethanol as shown in Fig. 2. In the former the salt appears to reduce the final intensity of light absorption and since the addition of lithium chloride to solutions of pure cinnamyl chloride in dimethylformamide results in a slow decrease to similar light-absorption intensities, it is

* In view of a comment by the Referees it must be emphasized that at no time did the late Professor Braude suggest that the presence of acid was a *necessary* condition for the isomeric rearrangement of allyl halides.

[14] Braude, *Ann. Reports*, 1949, **46**, 114; *Quart. Rev.*, 1950, **4**, 404.

conceivable that the position of equilibrium is affected, being no longer almost entirely in favour of the conjugated isomer. It has not been possible to prove this directly since the presence of unconjugated material cannot be detected in the product isolated after equilibrium is attained. An alternative explanation may be that the salt is merely catalysing a slow reaction between the organic halide and dimethylformamide such as has been observed by Kornblum and Blackwood.[15] It is perhaps significant that solutions of cinnamyl bromide in this solvent at 80° are considerably less stable than those of the chloride, and show a much larger decrease in light-absorption intensity on the addition of lithium bromide, but again only the cinnamyl isomer can be recovered.

Conductivity measurements indicate that in dimethylformamide the concentration of free chloride ion is not directly proportional to salt concentration over the range 0—0·5M, so we suggest that the linear increase in rate is unlikely to be due to a bimolecular reaction of 1-phenylallyl chloride with free chloride ion. If free chloride ions were involved the derived second-order rate constants (k_2) would decrease with salt concentration. Such a behaviour has been reported by England [3] for the rearrangement, kinetically of first

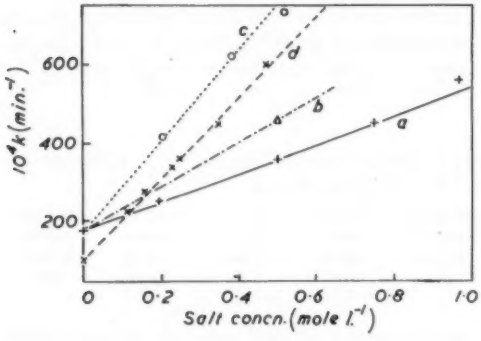


FIG. 2.

a Lithium chloride in ethanol at 25°.
b Lithium bromide in ethanol at 25°.
c Lithium azide in ethanol at 25°.
d Lithium chloride in dimethylformamide at 80°.

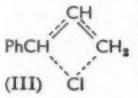
order, of 1-methylallyl bromide in the presence of lithium bromide (up to 0·1005M) in acetone. In view of the apparent discrepancy with our own results we have re-examined England's. He found that the rate of isomerization of the methylallyl bromides in the absence of salt is very slow and assumed that it could be neglected in calculating the rate in the presence of salt. England's second-order rate constants can be converted into first-order rate constants by multiplying them by the salt concentration and dividing by 0·75. These values, when plotted against salt concentration, give a reasonably straight line over the whole range used, which has an intercept of $0{\cdot}4 \times 10^{-5}$ sec.$^{-1}$ at zero salt concentration, considerably higher than the value of $0{\cdot}01$—$0{\cdot}1 \times 10^{-5}$ sec.$^{-1}$ which can be estimated for the rate constant of the spontaneous isomerization from England's data. Our observations thus accord with England's except that in our case the rate of the uncatalysed rearrangement falls on the straight line given by the rates in the presence of lithium chloride. In the reaction studied by England the rate plot may become sharply curved at very low salt concentrations ; in our example, owing perhaps to the presence of traces of hydrogen chloride, we may have been unable to measure the rate of the truly spontaneous rearrangement.

The effect of lithium bromide on the rate in ethanol is larger than that of the chloride, and the effect of the azide is yet larger (Fig. 2). Similar results are observed in dimethylformamide where the effect of azide is particularly pronounced. In the latter case the first-order rate constants fall during the run owing to the formation of cinnamyl azide which may be produced in an S_N2' reaction. However, catalysis of the isomerization

[15] Kornblum and Blackwood, *J. Amer. Chem. Soc.*, 1956, **78**, 4037.

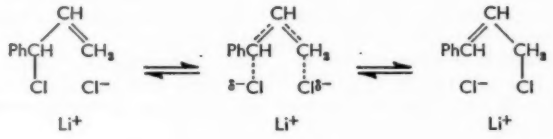
followed by very rapid S_N2 reaction of the cinnamyl chloride with lithium azide cannot be excluded for certain. Cinnamyl azide is also formed in ethanol, but the first-order rate constants of the rearrangement do not appear to decrease with time. Nevertheless it is clear that little if any 1-phenylallyl azide is formed in ethanol or in dimethylformamide since it should be relatively stable under the reactions conditions towards both solvolysis and rearrangement.

Mechanisms.—The variation of rate with ionizing power of the solvent suggests that, in aqueous dioxan at least, the rearrangement involves ionization of the C–Cl bond in the rate-determining step. Since solvolysis occurs independently to give largely the 1-phenylallyl products [10] we suggest that the chloride and carbonium ions are not separated by solvent molecules, *i.e.*, that formation of an ion-pair of the intimate type proposed by Winstein [4] is rate-determining. The much lower value of m obtained for the alcoholic solvents could indicate a different mechanism in these cases, namely, an S_Ni' reaction involving a transition state to which covalent structures such as (III) make an important contribution.



(III)

The rate increase in the presence of lithium chloride is, as previously remarked, unlikely to be due to an S_N2' reaction with halide ion of the type suggested by England.[3] It is conceivable that an S_N2' reaction with lithium chloride ion-pairs occurs in which the lithium ion acts as a bridge:



However the rate constant k_2 derived on this basis varies with ionizing power of the solvent in almost exactly the same way as does the rate constant of the uncatalysed rearrangement. This suggests that the salt is merely catalysing the unimolecular rearrangement and that even the modified S_N2' reaction does not occur. The increase in rate of the isomerization of 1,1-dimethylallyl chloride in aqueous ethanol due to added lithium chloride has been explained by de la Mare and Vernon [16] as due to salt catalysis. In the present case and particularly that of the methylallyl bromides the rate increase is much too large to be accounted for by an ionic-strength effect. On the other hand, from the variation of k_2 with temperature a value for E_A of about 26 kcal. mole^{-1} can be derived, about 7 kcal. mole^{-1} higher than for the uncatalysed reaction, and this suggests that a bimolecular reaction *is* involved. England found that E_A for the " S_N2' reaction " of the methylallyl bromides is larger than E_A for the S_N2 reaction by about 3 kcal. mole^{-1}. That lithium bromide and azide have larger effects on the rate than the chloride again suggests that a bimolecular displacement is involved, since nucleophilicity increases in the order $Cl^- < Br^- < N_3^-$. Clearly, the present evidence is insufficient to decide the mechanism of rearrangement in the presence of lithium salts.

Since in the presence of acids the increase in the rate of rearrangement is proportional to the stoicheiometric acid concentration and related to the strength of the acid, it is reasonable to suggest that one molecule of the acid associates with one molecule of the chloride so that the C–Cl bond is weakened. The nucleophilicity of an undissociated carboxylic acid is much lower than that of a chloride ion so that rearrangement remains essentially intramolecular; cinnamyl esters are not formed. Braude [14] suggested that a halonium ion analogous to an oxonium ion, might be formed under these conditions, but although information concerning the ionization of carboxylic acids in chlorobenzene is lacking we prefer the alternative explanation given.

[16] de la Mare and Vernon, *J.*, 1954, 2504.

Experimental

Analyses were by Miss J. Cuckney and the staff of the Organic Chemistry Microanalytical Laboratories. Infrared spectra were determined for liquid films by Mr. R. L. Erskine, B.Sc., A.R.C.S. Ultraviolet absorption data refer to cyclohexane solutions.

1-Phenylallyl Chloride.—To 1-phenylallyl alcohol (0·1 mole) and dry triethylamine (0·12 mole) in alcohol-free chloroform (150 ml.) at −10° was added with stirring over 25 min. thionyl chloride (0·11 mole) in alcohol-free chloroform (10 ml.). The solution was stirred for a further 10 min. and then quickly washed with water, aqueous sodium hydrogen carbonate, and water (all at 0°), and then dried (Na_2SO_4). The solvent was removed under vacuum at as low a temperature as possible and the crude *chloride*, n_D^{25} 1·5616, $\lambda_{max.}$ 2530 Å ($E_{1\,cm.}^{1\%}$ 660), rapidly distilled giving fractions: (i) b. p. 48—52°/0·4 mm. (0·4 g.), n_D^{22} 1·5448; (ii) b. p. 52—58°/0·4 mm. (2·2 g.), n_D^{22} 1·5475; (iii) b. p. 58—65°/0·35 mm. (1·0 g.), n_D^{22} 1·5682; (iv) b. p. 65—70°/0·35 mm. (1·1 g.), n_D^{22} 1·5805; (v) b. p. 70—72°/0·35 mm. (2·5 g.), n_D^{22} 1·5832. Fractions (i) and (ii) combined had $\lambda_{max.}$ 2530 Å (ε 3500), $\nu_{max.}$ 1636 (C=C), 983, 930 (−CH=CH_2), and 965 (*trans* −CH=CH−) cm.$^{-1}$ (Found: C, 70·5; H, 6·09; Cl, 22·6. C_9H_9Cl requires C, 70·8; H, 5·95; Cl, 23·3%). Alternatively the reaction mixture was worked up as follows: The washings were omitted and the solvent immediately removed at low temperature under vacuum. The chloride was extracted from the residue with pentane. After removal of the pentane, the crude product had n_D^{25} 1·5601, $\lambda_{max.}$ 2530 Å ($E_{1\,cm.}^{1\%}$ 640) and was practically identical with that above.

The refractive index and absorption intensity of samples prepared at various times varied somewhat, and the best sample, obtained after three distillations of material having initially b. p. 50—60°/0·35 mm., had n_D^{22} 1·5420, $\lambda_{max.}$ 2530 Å (ε 1900).

Samples were stored in stoppered tubes at −196°. A sample after being heated at 90° for 6 hr. (sealed tube) had n_D^{18} 1·5820, $\lambda_{max.}$ 2530 Å (ε 20,000) and an infrared spectrum identical with that of *trans*-cinnamyl chloride prepared by the action of thionyl chloride on *trans*-cinnamyl alcohol in ether.

Cinnamyl Trichloroacetate.—Trichloroacetyl chloride (4 g., from trichloroacetic acid and thionyl chloride) in dry benzene (10 ml.) was added in portions to cinnamyl alcohol (4 g.) in pyridine (3 g.) and dry benzene (50 ml.) at 0°. After storage at room temperature for 18 hr., pyridine hydrochloride was filtered off and the filtrate diluted with ether (100 ml.), washed with water and aqueous sodium hydrogen carbonate, and dried (Na_2SO_4). Distillation gave the *ester*, b. p. 101—103°/0·001 mm. (4 g.), n_D^{22} 1·5612, $\lambda_{max.}$ 2520 Å (ε 19,000), $\nu_{max.}$ 1785 cm.$^{-1}$ (C=O) (Found: C, 47·0; H, 3·44; Cl, 37·2. $C_{11}H_9O_2Cl_3$ requires C, 47·2; H, 3·22; Cl, 38·1%)

Rearrangement Products.—(*a*) The chloride (1·2 g., n_D^{22} 1·5499), trichloroacetic acid (1·2 g.), and chlorobenzene (15 ml.) were heated at 90° for 15 min. The cooled solution was diluted with ether, washed with aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and distilled. The product (0·8 g.) had n_D^{22} 1·5812, $\lambda_{max.}$ 2530 Å (ε 19,000), and an infrared spectrum identical with that of cinnamyl chloride. There was no residue. To show that cinnamyl trichloroacetate if formed would be stable under the reaction conditions, the ester (1·4 g.) was dissolved in chlorobenzene (50 ml.) saturated with hydrogen chloride (~0·6M) at room temperature, and heated at 90° for 10 min. (sealed tube). The mixture was worked up as before and the product (1·0 g.) had n_D^{19} 1·5612, $\lambda_{max.}$ 2520 Å (ε 19,000), and an infrared spectrum identical with that of cinnamyl trichloroacetate. No evidence of the presence of cinnamyl chloride was obtained. (*b*) The chloride (1·0085 g., n_D^{23} 1·5452), lithium chloride (0·107 g.), and *NN*-dimethylformamide (10 ml.) were heated at 80° for 3 hr. The solvent was removed by distillation and the residue extracted with light petroleum (b. p. 40—60°). The extract was washed with water, dried (Na_2SO_4), and distilled, giving a product (0·72 g.), b. p. 56°/0·05 mm., n_D^{22} 1·5814, $\lambda_{max.}$ 2530 Å (ε 20,600), with an infrared spectrum identical with that of cinnamyl chloride (Found: C, 70·6; H, 6·05; Cl, 22·7. Calc. for C_9H_9Cl: C, 70·8; H, 5·95; Cl, 23·3%).

Kinetic Measurements.—Solvents were carefully purified and dried by the following methods: Chlorobenzene was washed with aqueous sodium hydrogen carbonate, dried ($CaCl_2$), and distilled from a trace of sodium. *NN*-Dimethylformamide was kept for some days over sodium sulphate and then distilled under reduced pressure; this procedure was repeated three times. Dioxan was refluxed with sodium for 6—8 hr. and then distilled. Methanol was refluxed with magnesium (4 hr.) and then distilled. Propan-2-ol and 2-methylbutan-2-ol were

XUM

refluxed over calcium oxide (6 hr.) and then distilled. Burnett's absolute alcohol was not further purified. Lithium salts were freed from water by dissolution in ethanol followed by evaporation to dryness and heating at 100° *in vacuo*. Chloroacetic acids were redistilled.

The kinetic method previously described was employed,[17] the reaction being followed by measuring the absorption intensity at 2530 Å. Carboxylic acids and salts were added as accurately measured volumes of stock solutions.

First-order rate constants (k, min.$^{-1}$) are calculated from the expression,

$$k = (2{\cdot}3/t) \log_{10} [(a - x_0)/(a - x)],$$

where t is the time (min.), a is the final intensity, x_0 the initial intensity, and x the intensity of light absorption at time t. In media such as aqueous dioxan, the solvolysis of cinnamyl chloride is much slower than the solvolysis and isomeric rearrangement of 1-phenylallyl chloride; thus the calculated k represents the sum of the competing first-order reaction rate constants. The rate constant for isomeric rearrangement (k_r) is obtained by multiplying by the fraction of cinnamyl chloride produced, *i.e.*,

$$k_r = k [1 - cs/(c - x_0)]$$

where c is the light absorption intensity of pure cinnamyl chloride, and s the fraction of solvolysis. s was determined by adding 0·5 ml. of the reaction mixture at t_∞ to water (*ca.* 70 ml.) and light petroleum (*ca.* 30 ml.). The mixture was shaken and titrated with standard alkali, Methyl Red being used as indicator. Typical runs are in Table 4.

TABLE 4.

(a) *Rearrangement in chlorobenzene*, 90°. *Chloride concn.*, 0·332 *mole l.*$^{-1}$. *Trichloroacetic acid concn.*, 0·005 *mole l.*$^{-1}$.

t (min.)	0	10	15	20	27	40	55	∞	
$E^{1\%}_{1\,cm.}$	244	361	428	478	544	662	784	1200	
10^3k (min.$^{-1}$) ...	—	1·31	1·42	1·40	1·40	1·44	1·51	—	(mean 1·41)

(b) *Rearrangement and solvolysis in* 85% *aqueous dioxan*, 25°. *Chloride concn.*, 0·162 *mole l.*$^{-1}$.

t (min.)	0	4	5	8	10	15	69	
$E^{1\%}_{1\,cm.}$	290	375	400	450	480	560	1005	
10^3k (min.$^{-1}$) ...	—	3·12	3·22	3·16	3·08	3·17	—	(mean 3·15)

After 75 min. 0·5 ml. of reaction mixture required 0·54 ml. of 0·0377M-sodium hydroxide for neutralization, giving $s = 0{\cdot}251$ and $10^3k_r = 2{\cdot}14$ min.$^{-1}$.

(c) *Rearrangement in dimethylformamide in the presence of lithium azide*, 40°. *Chloride concn.*, 0·149 *mole l.*$^{-1}$. *Lithium azide concn.*, 0·21 *mole l.*$^{-1}$.

t (min.)	0	1	2	5	9	240	
$E^{1\%}_{1\,cm.}$	280	701	865	1050	1160	1270	
10^3k (min.$^{-1}$) ...	—	55·4	44·6	30·0	24·4	—	(extrap. ~75)

We are indebted to the late Professor E. A. Braude for advice and encouragement in the early stages of this work, and to Professor D. H. R. Barton, F.R.S., for criticism. One of us (G. V.) thanks the Greek State Scholarships Foundation for a Postdoctoral Research Scholarship.

DEPARTMENT OF CHEMISTRY,
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.7.

[*Received, February 26th*, 1959.]

[17] Braude and Jones, *J.*, 1944, 436 *et seq.*

XUM

546. *New Heteroaromatic Compounds. Part III.*[1] 2,1-*Borazaronaphthalene* (1,2-*Dihydro*-1-*aza*-2-*boranaphthalene*).

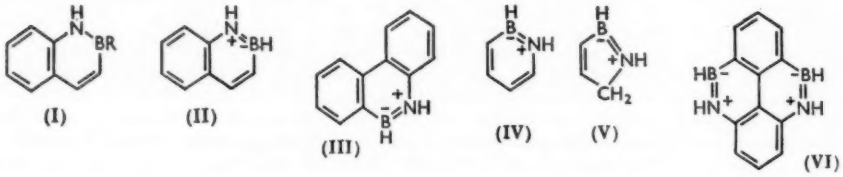
By M. J. S. Dewar and R. Dietz.

The synthesis of compound (II) and of some 2-substituted derivatives (I) is reported. The compounds show aromatic properties, and their spectra resemble those of corresponding naphthalene derivatives.

Nomenclature.—A nomenclature was desired which would take into account the fact that the group $-BH^{-}=NH^{+}-$ (equivalent to $-BH-NH-$) is isoconjugate with $-CH=CH-$ in an aromatic system. For instance, a name was desired which (*a*) would show that compound (I; R = H) (equivalent to II) is isoconjugate with naphthalene and (*b*) would not relate it to dihydronaphthalene as would strict systematic use of azabora-prefixes.* After consultation with the Editor, the prefix " aro " has been adopted, to be placed between the -a prefixes and the name of the cyclic hydrocarbon with which the compound is isoconjugate. Thus, compound (I; R = H) is named 2,1-borazaronaphthalene. For six- and five-membered rings the composite suffixes -arene and -arole, respectively, are proposed. The following are further examples: (III) 9,10-borazarophenanthrene; (IV) 1,2-borazarene; (V) 1,2-borazarole; (VI) 4,10-dibora-5,9-diazaropyrene.

Previous papers in this series recorded boron compounds isoconjugate with indole, 2 : 3-benzofuran, thionaphthen,[1] and phenanthrene.[2] In this paper a new heteroaromatic system isoconjugate with naphthalene is described.

Reaction of 2-aminostyrene with boron trichloride in benzene in the absence of a catalyst gave hydrogen chloride and a white, sublimable solid, containing chlorine, which was hydrolysed with extreme ease. This chloro-compound with phenylmagnesium bromide gave a compound $C_{14}H_{12}NB$, identical with the product of the direct reaction



between phenylboron dichloride and 2-aminostyrene. The stability of this compound towards hot dilute alkali and cold potassium permanganate, its methods of preparation, and its spectral similarity to 2-phenylnaphthalene (Fig. 1) show it to be the isoconjugate compound 2-phenyl-2,1-borazaronaphthalene (I; R = Ph). The chloro-compound is therefore the 2-chloro-compound (I; R = Cl).

Hydrolysis of the chloro-compound gave bis-2,1-borazaronaphthyl ether and not the expected 2-hydroxy-compound (I; R = OH). The absence of a hydroxyl group was

* It is regretted that, owing to incorrect editorial advice, compounds such as (II) and (III) were incorrectly named in earlier Parts of this series.[1,2] For instance, compound (III) was there termed 9-aza-10-boraphenanthrene whereas, whether the Stelzner or the *Chemical Abstracts* system is used,[3] it should be regarded as an azabora-derivative of dihydrophenanthrene. Compounds (I) are similarly systematically named as derivatives of dihydronaphthalene. It is unnecessary to list the other errors from the earlier papers.

[1] Part II, Dewar, Kubba, and Pettit, *J.*, 1958, 3076.
[2] Part I, *Idem*, *J.*, 1958, 3073.
[3] " I.U.P.A.C. Nomenclature of Organic Chemistry, 1957," Butterworths, London, 1958, rule B-4.1, pp. 65—67.

confirmed by the infrared spectrum, and the fact that the compound was soluble in alkali only on prolonged boiling.

Reduction of the chloro-compound with lithium aluminium hydride gave the parent substance (I; R = H). With methylmagnesium iodide, the chloro-compound gave the methyl derivative.

The aromaticity of these compounds is evident in their spectral similarity to naphthalene derivatives and in their general stability, which is greater than the classical formula (I) would suggest. The insolubility of the ether in cold alkali is incompatible with its formulation as an anhydride of a boronous acid, and its stability to boiling alkali (Fig. 2) indicates that the compounds do not behave as cyclic boron amides. The unusual stability of the parent compound, a boron hydride, to hydrolysis is shown by the similarity of the spectra measured in cyclohexane and in 95% ethanol, even in the presence of acids (Fig. 3). The aromatic nature of the compounds is emphasised by the dipolar Kekulé structure (II). Structure (I; R = H) is, of course, more important than the corresponding excited structure of naphthalene.

FIG. 1. FIG. 2. FIG. 3.

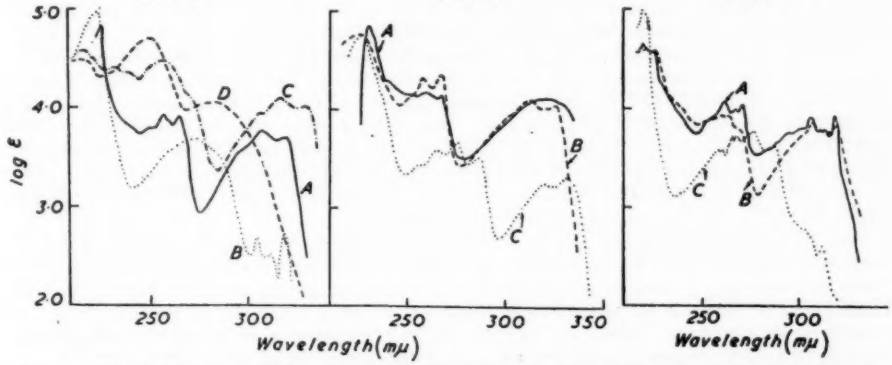


FIG. 1. *Ultraviolet spectra of* (*A*) *2-methyl-2,1-borazaronaphthalene and* (*B*) *2-methylnaphthalene in alcohol, and of* (*C*) *2-phenyl-2,1-borazaronaphthalene and* (*D*) *2-phenylnaphthalene in cyclohexane.*

FIG. 2. *Ultraviolet spectra of* (*A*) *bis-2,1-borazaro-2-naphthyl ether in* 10% *aqueous alkali after boiling and* (*B*) *in cyclohexane, and* (*C*) *of 2-naphthol in alcohol.*

FIG. 3. *Ultraviolet spectra of* 2,1-*borazaronaphthalene* (*A*) *in cyclohexane and* (*B*) *in alcohol with acid, and* (*C*) *of naphthalene in cyclohexane.*

The main absorption bands of 2,1-borazaronaphthalene correspond closely to those of naphthalene (Fig. 3), but the intensity of the α-bond (320 mμ region) is much greater. A similar phenomenon was observed in the case of 9,10-borazarophenanthrene and explained in terms of molecular-orbital theory.[2] That the spectrum of bis-2,1-borazaronaphthyl ether is little changed in aqueous alkali would be expected since conjugation between boron and oxygen is strong and is little affected by the electronic configuration of the oxygen atom.

The mild conditions under which these compounds are formed suggest that other suitably substituted ethylenes would condense with boron derivatives. An investigation of these reactions is in progress.

EXPERIMENTAL

Boron analyses were carried out by the volumetric method developed by Leigh, Fowler, and Kraus.[4] Molecular weights were determined by freezing-point depression in naphthalene. M. p.s are corrected.

[4] Leigh, Fowler, and Kraus, *J. Amer. Chem. Soc.*, 1940, **62**, 1143.

2-Aminostyrene was prepared from phenethyl alcohol.[5]

Bis-2,1-borazaro-2-naphthyl Ether.—A solution of 2-aminostyrene (1 g.) in dry benzene (40 ml.) was added slowly with stirring to a solution of boron trichloride (2 g.) in benzene (10 ml.) at room temperature. The mixture was boiled under reflux for 3 hr. The solvent was distilled off, and the residue crystallised from light petroleum to give the *ether* as colourless plates (0·51 g., 45%), m. p. 198—200° (Found: C, 70·1; H, 5·1; N, 10·3; B, 7·8. $C_{16}H_{14}ON_2B_2$ requires C, 70·6; H, 5·2; N, 10·3; B, 8·0%).

2-Chloro-2,1-borazaronaphthalene.—The previous experiment was repeated, and the solvent removed with exclusion of moisture. From the residue, *2-chloro-2,1-borazaronaphthalene* sublimed at 60—65°/0·3 mm., in needles, m. p. 72—74°. Direct hydrolysis and titration with alkali gave Cl, 19·6% as a maximum value (C_8H_7NBCl requires Cl, 21·7%). Professional analyses of this compound gave very low chlorine values, and correspondingly high carbon, hydrogen, and nitrogen values. Hydrolysis is obviously rapid.

2,1-Borazaronaphthalene.—A solution of lithium aluminium hydride (0·5 g.) in dry ether was added in ½ hr. to a solution of crude 2-chloro-2,1-borazaronaphthalene (from 1 g. of 2-aminostyrene) in dry ether, between −5° and 0°. The mixture was stirred for 2 hr. at room temperature. Moist ether was added, and the solution filtered and evaporated to dryness. From the residue there sublimed at 80°/0·6 mm. a white solid, which, crystallised from light petroleum, gave *2,1-borazaronaphthalene* (0·42 g., 40%), m. p. 100—101° (Found: C, 74·5; H, 6·2; N, 10·9; B, 7·9. C_8H_8NB requires C, 75·0; H, 6·3; N, 10·9; B, 8·4%).

2-Phenyl-2,1-borazaronaphthalene.—(a) *From phenylboron dichloride.* A solution of 2-aminostyrene (2 g.) in dry benzene (20 ml.) was added dropwise and with constant stirring to one of phenylboron dichloride (2·7 g.) in dry benzene (10 ml.) at room temperature in ½ hr. The mixture was then boiled under reflux for 2 hr. On cooling, a white solid was precipitated. Ether was added, and the solution washed with dilute aqueous sodium carbonate, dried, and evaporated. Crystallisation from light petroleum gave *2-phenyl-2,1-borazaronaphthalene* in colourless plates (2·1 g., 69%), m. p. 137·5—139° (Found: C, 81·7; H, 6·1; N, 6·7; B, 5·1%; *M*, 205. $C_{14}H_{12}NB$ requires C, 81·9; H, 5·9; N, 6·8; B, 5·3%; *M*, 208).

(b) *By a Grignard reaction.* To a solution in dry ether of crude 2-chloro-2,1-borazaronaphthalene (from 1 g. of 2-aminostyrene) was added slowly one of phenylmagnesium bromide [from magnesium (1 g.) and bromobenzene (6·8 g.)], with ice-cooling in ¾ hr. The mixture was stirred for 2 hr. at room temperature and boiled under reflux 1 hr. Water was added and the organic layer separated, dried, and evaporated. Crystallisation from light petroleum gave 2-phenyl-2,1-borazaronaphthalene (0·65 g., 43%), m. p. and mixed m. p. 138—139°.

2-Methyl-2,1-borazaronaphthalene.—A similar Grignard reaction gave a 45% yield of *2-methyl-2,1-borazaronaphthalene*, crystallising in plates (from light petroleum), m. p. 73—74° (Found: C, 74·3; H, 7·3; N, 9·8; B, 7·3%; *M*, 137. $C_9H_{10}NB$ requires C, 75·6; H, 7·1; N, 9·8; B, 7·6%; *M*, 143).

One of us (R. D.) thanks the British Petroleum Company for a Research Studentship; we are also grateful to the University of London for a grant for the purchase of apparatus.

CHEMISTRY DEPARTMENT, QUEEN MARY COLLEGE,
MILE END ROAD, LONDON, E.1. [*Received, November 18th*, 1958.]

[5] Sabetay, Bleger, and de Lastrange, *Bull. Soc. chim. France*, 1931, **49**, 3.

547. *Diffusion Studies with Phosphatide Sols.*

By I. L. Thomas and L. Saunders.

Integral and semi-differential diffusion studies have been performed with mixed sols of lecithin and lysolecithin. The diffusion of the phosphatides followed the theory for the diffusion of a single solute. The value of the diffusion coefficient decreased rapidly as the weight fraction of lecithin was increased. Calcium chloride had some effect on the diffusion rate.

Phosphatides are important constituents of cell membranes. Lecithin is present in most cell membranes, but the presence of lysolecithin has not been proved. However lysolecithin is very likely to be present since lecithinase A enzyme, which specifically hydrolyses lecithin to lysolecithin, is widely distributed in the body. Studies of the physical properties of mixed aqueous sols of these materials should help in the elucidation of the structure and mechanism of formation of cell membranes.

We showed previously[1] that lysolecithin existed in aqueous sols as large, fairly uniform micelles and that the diffusion rate of the lysolecithin was unaffected by calcium chloride. Details are here given of the diffusion of mixed sols of lecithin and lysolecithin, and the effect of calcium chloride on the diffusion rate.

Experimental

The diffusion rate was measured by using a Gouy diffusiometer.[2,3] The photographing of the Gouy patterns was made wholly automatic. The photographic plate, in a carrier, was moved by an electric motor *via* a rack and a one-tooth pinion, so that one revolution (½ hr.) of the pinion moved the rack ¼ in. The shutter, at one side of the thermostat bath containing the diffusion cell, was controlled by a time switch so adjusted that a photograph was taken every ½ hr., and the exposure times could be varied. Photographs were taken only whilst the plate was stationary.

Materials.—Lysolecithin was prepared as described previously.[1] Lecithin was prepared as described by Saunders.[4] "AnalaR" calcium chloride was used.

Preparation of the Sols.—Small quantities of the alcoholic stock solutions of lecithin and lysolecithin were evaporated to dryness under vacuum, and weighed quantities of each substance were placed in the same sample flask. A small quantity of ethyl alcohol was added and upon gentle warming a clear solution was obtained. This alcoholic solution was evaporated to dryness under vacuum, leaving a residue of intimately mixed phosphatides. A small volume of distilled water was added and the flask was attached to an automatic shaking machine and placed in a water-bath whose temperature was kept below 55°. The flask was shaken until a clear sol was obtained. In order to remove any electrolytes present as impurities the sol was then passed over a bed of mixed ion-exchange resins consisting of 0·25 g. of Amberlite Resin IR-120(H) and 0·4 g. of Amberlite Resin IRA-400(OH). Small successive quantities of distilled water were passed over the ion-exchange resins to remove any adherent phosphatide. The sol was finally made up to volume with distilled water.

Preparation of sols containing calcium chloride. A mixed phosphatide sol was prepared as above, except that its concentration was twice that required finally. To this was added an equal volume of calcium chloride solution of twice the final concentration required. All concentrations (C) are expressed as percentage (w/v).

Integral Diffusion.—With all the integral diffusion experiments with mixed phosphatide sols, the C_t values obtained on analysing any Gouy pattern were constant, but the apparent coefficient (D) decreased with increased time of diffusion. On plotting D against $1/t$ a straight line was obtained, and the true value of D was obtained by extrapolation to $1/t = 0$.[2] The values so obtained for D were not very consistent; its value decreased rapidly as the proportion of lecithin in the mixture was increased.

[1] Saunders and Thomas, *J.*, 1958, 483.
[2] Saunders, *J.*, 1953, 519.
[3] Brudney and Saunders, *J.*, 1955, 2916.
[4] Saunders, *J. Pharm. Pharmacol.*, 1957, **9**, 834.

Good boundaries were formed quite readily with mixed sols having a total phosphatide concentration of 2% and a weight fraction of lecithin of 0·2 or less. With sols having a weight fraction of lecithin between 0·2 and 0·3 much greater difficulty was experienced, whilst with sols having a weight fraction between 0·3 and 0·6 it was impossible to form good boundaries. These difficulties are explained in the Discussion. With a sol having a weight fraction of lecithin of 0·6 light passed through the sol initially, but within 2 hr. of the commencement of diffusion, the sol close to the boundary started to become opaque, and this opacity spread rapidly throughout the sol. The boundary remained perfectly sharp even after four days, and no Gouy patterns were obtained on the photographic plate. On examining the sol after the experiment was completed, the opacity was found to be due to a white gelatinous coagulate. A similar result was obtained with a sol having a weight fraction of lecithin of 0·65, but in this case much longer elapsed before it became opaque.

No experiments were carried out with sols having a higher lecithin weight fraction than 0·65, since they were not optically clear.

Semi-differential Diffusion.—The boundaries formed between mixed phosphatide sols of different concentrations were so sharp that the diffusion coefficient varied only randomly with the time of diffusion, and so no extrapolation was necessary to obtain the true value of D. An analysis of three Gouy patterns obtained on the semi-differential diffusion of a 1·5% mixed phosphatide sol into a 0·3% mixed sol, each sol containing a weight fraction of lecithin of 0·15, is in Table 1. In Table 2 are the values of D obtained from five Gouy patterns on repeating the experiment twice.

TABLE 1.

	t = 13,500 sec.		t = 22,500 sec.		t = 27,900 sec.	
j	Y	C_t	Y	C_t	Y	C_t
1	1·7360	1·916	1·3423	1·482	1·2047	1·330
2	1·6714	1·910	1·2940	1·479	1·1623	1·328
3	1·6179	1·912	1·2514	1·479	1·1252	1·330
4	1·5692	1·911	1·2158	1·481	1·0915	1·329
5	1·5219	1·912	1·1773	1·479	1·0593	1·331
6	1·4798	1·912	1·1448	1·479	1·0287	1·329
7	1·4396	1·914	1·1137	1·481	1·0015	1·332
8	1·3999	1·912	1·0834	1·480	0·9741	1·331
9	1·3610	1·914	1·0540	1·482	0·9472	1·332
10	1·3258	1·913	1·0268	1·482	0·9232	1·332
S	0·0014		0·0014		0·0017	
10^7D	$6{\cdot}13_1$		$6{\cdot}14_0$		$6{\cdot}13_2$	

S = standard deviation of the C_t values.
Definitions of the terms used in the above Table have been given in an earlier paper.[3]

TABLE 2.

Number of expt.	10^7D				
1	$5{\cdot}91_2$	$5{\cdot}91_9$	$5{\cdot}92_9$	$5{\cdot}93_1$	$5{\cdot}92_9$
2	$6{\cdot}13_1$	$6{\cdot}14_0$	$6{\cdot}14_8$	$6{\cdot}13_2$	$6{\cdot}02_7$
3	$5{\cdot}92_0$	$5{\cdot}90_4$	$5{\cdot}90_3$	$5{\cdot}89_2$	$5{\cdot}94_6$

When semi-differential diffusion experiments were performed with sols containing varying weight fractions of lecithin, it was found that good boundaries were formed with all sols containing a weight fraction of lecithin of 0·3 or less, but with sols having a weight fraction greater than 0·3 it was impossible to form good boundaries. The diffusion coefficients for the mixed sols with weight fractions of lecithin below 0·3 are given in Table 3.

TABLE 3.

Wt. frac. of lecithin	0	0·100	0·150	0·200	0·250	0·300
10^7D	$6{\cdot}50_2$	$6{\cdot}32_2$	$5{\cdot}98_5$	$3{\cdot}90_2$	$2{\cdot}12_2$	$1{\cdot}30_4$

Effect of calcium chloride on the semi-differential diffusion rate of lecithin–lysolecithin sols. In Table 4 is given an analysis of three Gouy patterns obtained when a 1·5% mixed phosphatide sol was allowed to diffuse into a 0·3% mixed sol. The weight fraction of lecithin in each sol was 0·15, and the concentration of calcium chloride in both sols was 10^{-6}M. In Table 5 are given the semi-differential diffusion coefficients obtained when 1·5% mixed phosphatide sols were allowed to diffuse into 0·3% mixed sols in the presence of various concentrations of calcium chloride.

TABLE 4.

	t = 18,000 sec.		t = 23,400 sec.		t = 28,800 sec.	
j	Y	C_l	Y	C_l	Y	C_l
1	1·6424	1·819	1·4394	1·594	1·2997	1·439
2	1·5803	1·816	1·3882	1·596	1·2524	1·440
3	1·5293	1·812	1·3426	1·591	1·2088	1·432
4	1·4818	1·814	1·2978	1·588	1·1723	1·435
5	1·4376	1·815	1·2609	1·592	1·1361	1·434
6	1·3966	1·816	1·2219	1·589	1·1040	1·436
7	1·3549	1·814	1·1870	1·589	1·0729	1·436
8	1·3169	1·814	1·1550	1·591	1·0433	1·437
9	1·2799	1·815	1·1223	1·592	1·0158	1·441
10	1·2460	1·816	1·0940	1·595	0·9869	1·439
S	0·0017		0·0028		0·0028	
10^7D	$4·77_1$		$4·77_3$		$4·75_9$	

TABLE 5.

$[CaCl_2]$ (M) in upper and lower sols ...	0	10^{-8}	10^{-7}	10^{-6}	10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}
10^7D	5·98	5·92	5·70	4·76	5·66	5·76	5·50	5·04	4·07

DISCUSSION

The difficulties encountered in forming boundaries between sols containing various weight fractions of lecithin can be explained by our results of viscosity experiments.[5] With sols having a weight fraction of lecithin of 0·2 or less, the particles present are roughly spherical since the ratio of the specific viscosity to the volume fraction occupied by the phosphatides remains constant with increasing concentration. With sols having weight fractions of lecithin of 0·4 or 0·6 the particles are very asymmetric since this ratio increases rapidly with increasing concentration of phosphatides. The presence of these highly asymmetric particles in sols having weight fractions of lecithin 0·3—0·6 explains why they flowed anomalously, making it impossible to form good boundaries.

TABLE 6.

Wt. frac. of lecithin	Molar volume of micelle (10^{-5} c.c.)	Volume of one micelle (in 10^5 Å^3)	No. of molecules in each micelle
0	1·315	2·18	279
0·10	1·430	2·38	288
0·15	1·685	2·80	330
0·20	6·081	11·0	1160
0·25	37·8	62·8	7070
0·30	163	271	29,700

The results of integral diffusion experiments with sols having weight fractions of lecithin of 0·6 and 0·65 are very interesting. The white gelatinous coagulate, which does not diffuse, may be a molecular complex between lecithin and lysolecithin. (A sol having a weight fraction of lecithin of 0·6 contains an equimolecular mixture of the two phosphatides.)

The Gouy patterns from all experiments with mixed phosphatides sols, even in the presence of calcium chloride, were regular, and C_l's for any particular pattern were very constant (Tables 1 and 4). We infer that the diffusion of the mixed phosphatides alone, or in the presence of calcium chloride, follows the theory for the diffusion of a single solute. This indicates that in a particular sol the micelles are of fairly uniform size and shape.

With both the integral and semi-differential diffusion results, the diffusion rate of the mixed phosphatides decreases as the proportion of lecithin in the sol is increased, indicating that the micellar size is increasing. Assuming the micelles to be spherical, and our viscosity results with a sol having a weight fraction of 0·2 indicate this, we can calculate the size of the micelles by using the Stokes–Einstein equation. The results are in Table 6.

[5] Thomas and Saunders, *J. Pharm. Pharmocol.*, 1958, **10**, T182

With sols having a weight fraction of lecithin of 0·25 or 0·3 the particles are probably asymmetric.

Table 2 shows that on repetition of the same experiment the results showed some scatter, so they have been analysed statistically.

The variance of the values of D (Table 2) about their mean was estimated as $1{\cdot}00 \times 10^{-16}$, giving a standard deviation of $1{\cdot}00 \times 10^{-8}$ with fourteen degrees of freedom. The limits of error of a mean diffusion coefficient, calculated from five Gouy patterns, were estimated as $\pm 0{\cdot}133 \times 10^{-7}$ at the 0·99 probability level. The mean value of D was $5{\cdot}984 \times 10^{-7}$, and so these limits expressed as a percentage of the mean are $\pm 2{\cdot}22$.

To test whether various concentrations of calcium chloride were significantly reducing the diffusion rate of the phosphatides, the t-test of significance was applied to all the diffusion coefficients obtained for the phosphatides in the presence and absence of calcium chloride. Values for t are given in Table 7.

TABLE 7.

$[CaCl_2]$ (M)	10^{-8}	10^{-7}	10^{-6}	10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}
t	1·23	5·26	24·6	5·82	4·15	9·23	18·3	36·7

The theoretical t at the 0·95 probability level and with eighteen degrees of freedom is 2·11. Therefore a significant reduction in the diffusion rate of the phosphatides occurred with all the concentrations of calcium chloride used except 10^{-8}M. The marked fall in the diffusion rate of the phosphatides in the presence of 10^{-6}M-calcium chloride is probably due to bonding between the calcium ions and the negatively charged phosphate groups of the lecithin molecules from different micelles causing a linking of the micelles. The fall in the diffusion rate with high concentrations of calcium chloride is probably due to salting out, the high concentration of salt causing dehydration of the particles, thus facilitating aggregation.

The fact that there are two regions where the diffusion rate falls fits Malquori's observation [6] that small calcium concentrations flocculated lecithin sols, intermediate ones peptised them, and still larger ones caused flocculation again. Elworthy and Saunders [7] have also reported two maxima in the surface force–calcium chloride concentration curve for lecithin sols.

SCHOOL OF PHARMACY, UNIVERSITY OF LONDON,
BRUNSWICK SQUARE, LONDON, W.C.1.

[*Received, March 2nd,* 1959.]

[6] Malquori, *Atti IV Congr. naz. Chim. pura applicata*, 1932, 752.
[7] Elworthy and Saunders, *J.*, 1957, 330.

---

548. *Homolytic Substitution at a Saturated Carbon Atom. Part I. Products of the Gaseous Nitration of t-Butylbenzene.*

By H. C. DUFFIN, E. D. HUGHES, and SIR CHRISTOPHER INGOLD.

Existing evidence is equivocal as to whether alkyl radicals intervene in aliphatic nitration in the liquid or the gas phase by aqueous nitric acid or by nitrogen dioxide. This question is tested by a study of the gas-phase nitration of t-butylbenzene by these reagents, because the alkyl radical of that hydrocarbon, the 2-methyl-2-phenylpropyl (neophyl) radical, is one of the few alkyl radicals known to be capable of an internal rearrangement, by which, we hoped, it might disclose itself. Products of its rearrangement were found.

ALTHOUGH the classification of bonding electrons as σ and π is often criticised as inadequate, it is striking that the most typical and powerful electrophilic substituting agents, such as the chlorine molecule, the chlorinium ion, and the nitronium ion, which

characteristically substitute at aromatic and other π-electron centres, make no headway at all against carbon σ-electrons. In order to chlorinate or nitrate an alkane we must employ materials containing or producing other substituting agents, *e.g.*, for chlorination, partly atomised chlorine, and for nitration, nitrogen dioxide or dilute nitric acid.

Among these reactions, chlorination is especially well investigated as to mechanism. It is amenable to kinetic study, and, with guidance from prior work on the chlorine–hydrogen reaction, finally interpreted by the chain mechanism of Nernst, the chlorine–alkane reaction has kinetically been established as an analogous radical-propagated chain-process. However, as regards the substitutions which put into alkanes those groups which the typical electrophilic substitutions so easily introduce at aromatic centres, the kind of certainty about mechanism that can be secured by kinetic investigation ends with halogenation.

The nitration of alkanes is in a very different position. It has not yet been found possible to investigate it kinetically, mainly because of difficulties arising from concurrent oxidation with degradation. The only observations available to serve as evidence of mechanism relate to the nature of the products. Therefore, present ideas on mechanism are either vague or not agreed. It is widely thought that the reaction probably involves radicals, but views vary as to how these arise, what they all are, what happens to them, and, in particular, whether or not they carry forward a chain process.

In studying the mechanism of aliphatic nitration, our approach is to seek unequivocal answers to certain very limited questions first, in the hope that several such answers will make clear enough what is waiting to be proved to enable a confirmatory investigation to be designed. In this paper we investigate the validity of the idea that the mechanism depends on the extraction of a hydrogen atom from the alkane to give an alkyl radical. We must explain how the historical situation leads to this first question.

The nitration of alkanes (including cycloalkanes) with concurrent oxidation by dilute nitric acid at its boiling point or at higher temperatures under pressure (concentrated acid effecting only oxidation under such conditions) has been known since 1880.[1] A more modern phase of investigation of alkane nitration was initiated by Hass and his co-workers in 1936,[2] who used vapour flow at temperatures above, sometimes very much above, 150°, and concluded that reaction took place in the vapour, because silica gel exerted no catalysis. They employed two nitrating agents, namely, somewhat concentrated aqueous nitric acid and dinitrogen tetroxide, and claimed the same products from both, but better conversions from the former. The products consisted of a mixture of all the mononitro-compounds that could be formed by introducing a nitro-group in place of any hydrogen atom or any lower alkyl radical, in the original alkane; also of all the aldehydes or ketones that could result from oxygen uptake where a lower alkyl radical had been split off, together with various products of their further oxidation. The ease of replacement of the different types of hydrogen was in the order tertiary > secondary > primary at lower temperatures, with a shift towards equality at higher temperatures. No rearrangement of a carbon skeleton was observed; Hass was so impressed by this that he made it the first of the thirteen " rules " in which he summarised his findings.

One of the theories[3] considered during this work was that free radicals, thermally produced from the reagent, extracted hydrogen from the alkane to leave an alkyl radical, which then picked up a nitro-radical from the reagent. It was subsequently noticed[4] that added nitric oxide reduced conversion, whilst added oxygen and, as Bachman and his co-workers,

[1] Beilstein and Kurbatov, *Ber.*, 1880, **13**, 1818, 2028. Cf. Ellis, " The Chemistry of Petroleum Derivatives," Chemical Catalog Co., Inc., New York, 1937, vol. 2, p. 1087.

[2] Hass, Hodge, and Vanderbilt, *Ind. Eng. Chem.*, 1936, **28**, 339; Hass and Paterson, *ibid.*, 1938, **30**, 67; Seigl and Hass, *ibid.*, 1939, **31**, 648; Hibsham, Pierson, and Hass, *ibid.*, 1940, **32**, 427; Hass, Dorsky, and Hodge, *ibid.*, 1941, **33**, 1138; Hass and Riley, *Chem. Rev.*, 1943, **32**, 376; Hass, *Ind. Eng. Chem.*, 1943, **35**, 1146; Hass and Howe, *ibid.*, 1946, **38**, 251; Hass and Shechter, *ibid.*, 1947, **39**, 817.

[3] McCleary and Degering, *Ind. Eng. Chem.*, 1938, **30**, 64; Hass and Paterson, *ibid.*, p. 67.

[4] Hass and Alexander, *Ind. Eng. Chem.*, 1949, **41**, 2266.

XUM

showed,[5] added chlorine increased it. It was inferred that nitric oxide retards by destroying radicals, and that oxygen and chlorine accelerate either by creating them, or at least by destroying the nitric oxide formed in the oxidation which accompanies nitration. Thus the more definite picture emerged that nitrogen dioxide molecules from dinitrogen tetroxide, or nitrogen dioxide and a free hydroxyl radical, formed by the homolysis of nitric acid, $HNO_3 \longrightarrow OH + NO_2$, extract alkane hydrogen; and that the alkyl radical thus formed either combines with preformed nitrogen dioxide or extracts it from the reagent, leaving, if this is nitric acid, a hydroxyl radical, which, in collaboration with the alkyl radical, carries forward the propagation steps of the chain reaction:

$$RH + OH \longrightarrow R + H_2O$$
$$HNO_3 + R \longrightarrow OH + RNO_2$$

The obvious chain-terminating step is the radical combination,

$$R + NO_2 \longrightarrow RNO_2$$

Bachman added the suggestion that some of the nitrogen dioxide combines through oxygen to form an alkyl nitrite, which, by pyrolysis in the accepted way[6] to nitric oxide, a carbonyl compound, and a lower alkyl radical,

$$R'_2C{\cdot}ONO \longrightarrow R' + R'_2CO + NO$$

leads to the oxidation products and the lower nitro-compounds.

Plausible as these suggestions seem, they have been attacked at two vital points. Stevens and Schiessler[7] nitrated optically active 3-methyloctane by heating it with dilute nitric acid under pressure; they obtained an optically active 3-methyl-3-nitro-octane. They therefore preferred to assume a bimolecular exchange of radicals in a synchronous homolytic process, rather than any step-wise mechanism involving the intermediate production of a free alkyl radical. Fréjacques[8] showed that the pyrolysis of nitric acid vapour at 280—380° is of second order, and is therefore not rate-controlled by the assumed unimolecular homolysis to hydroxyl and nitroxyl radicals, but might be by a bimolecular dehydration to water and dinitrogen pentoxide, the latter being instantly converted, as it would be at the temperatures used, into the other final products of the pyrolysis, namely, nitrogen dioxide and oxygen. Fréjacques also showed that, in a mixture of nitric acid and methane, pyrolysis of the former was concluded long before nitration of the latter was, and hence that the nitration could not depend on nitric acid molecules, as the hypothetical chain-reaction made it, but must be effected by some product of the pyrolysis of nitric acid. Thus the most widely considered concept of aliphatic nitration, the chain mechanism, has been doubly undermined, inasmuch as both the short-lived radicals on which it relies, alkyl and hydroxyl, have been questioned. This paper is concerned with the alkyl radical.

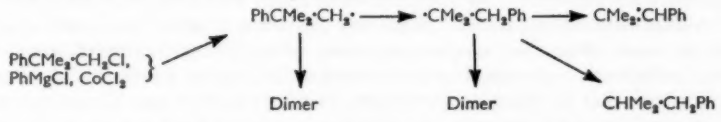
The test we have employed for the validity of this intermediate is equally one of the predictive power of Hass's rule that in aliphatic nitration the carbon skeleton is not rearranged. A necessary condition[9] for rearrangement in a reaction of a saturated carbon system is the formation of an intermediate with an incomplete electron shell, and therefore of either a carbonium ion or a neutral carbon radical. This mechanistic condition, though necessary, is not sufficient, for the thermodynamic condition, that the free-energy change must be in the right direction, has also to be satisfied; so has the kinetic condition that the intermediate must live long enough to allow for the group migration. Only if all three conditions are fulfilled shall we observe rearrangement. Therefore, if we do not observe it, we can conclude nothing about mechanism; if we do, then we shall have established the formation of an intermediate with an electron-deficient centre.

[5] Bachman, Addison, Hewett, Kohn, and Millikan, *J. Org. Chem.*, 1952, **17**, 906.
[6] Rice and Radovskas, *J. Amer. Chem. Soc.*, 1935, **57**, 350.
[7] Stevens and Schiessler, *J. Amer. Chem. Soc.*, 1940, **62**, 2885.
[8] Fréjacques, *Mém. Poudres*, 1953, **35**, appendix.
[9] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, New York, 1953, Chap. 9.

XUM

Rearrangements by way of a carbonium ion have a very large literature, and are obviously much easier to realise than rearrangements by way of a carbon radical, which have a very small one. Probably the kinetic condition, that the life of the intermediate must be longer than the time required for rearrangement, is much more easily satisfied in carbonium ions than it is in radicals.[10] The idea that alkyl radicals are intermediates in alkane nitrations could probably be reconciled with Hass's non-rearrangement rule on the basis that rearranging radicals are sufficiently uncommon to make it likely that none of the hydrocarbons which he nitrated would have produced one. However, radicals can be produced which can gain such stability by the internal migration of a sufficiently mobile group that an observable amount of rearrangement occurs during their lifetime. We therefore sought a hydrocarbon which by hydrogen loss would yield such a radical, planning to nitrate it under such conditions that, if formed, the alkyl radical could live long enough to permit observable rearrangement, and would therefore disclose itself by the formation of rearrangement products.

The simplest well-authenticated radical of the required kind is the 2-methyl-2-phenylpropyl (neophyl) radical, which Urry and Kharasch produced by reduction of the chloride with a Grignard reagent and cobaltous chloride.[11] They showed that they had made the radical by isolating its dimer, and that part of it is rearranged in their conditions to the presumably more stable 1-benzyl-1-methylethyl radical by isolating the dimer of that also. The non-dimerised reaction products were simple redox derivatives, ωω-dimethylstyrene and 2-benzylpropane, of the rearranged radical:



Our choice of a hydrocarbon for this study of aliphatic nitration therefore fell upon t-butylbenzene, which, by loss of an alkyl hydrogen atom, can only give the 2-methyl-2-phenylpropyl radical. Using the vapour-flow method, we have examined its reaction with aqueous nitric acid and with nitrogen dioxide in the gas phase between 200° and 350°, particularly at and near 325°.

At the outset there was doubt as to whether our plan would be frustrated by nuclear nitration. Ordinary electrophilic nitration in the ring of t-butylbenzene is nearly as fast as in that of toluene, whereas any homolytic replacement of side-chain hydrogen in t-butylbenzene is expected to be considerably slower than in toluene, and hence more easily masked by a competing nuclear nitration. Reports on the gas-phase nitration of toluene with aqueous nitric acid were equivocal, Bullock and Mitchell [12] having claimed the production of nitrotoluenes in this way, whereas Hass and Riley [13] reported a number of products of attack on the side-chain, including nitrobenzene, but no nitrotoluene. As to liquid-phase nitration, Titov [14] heated toluene with dinitrogen tetroxide under pressure, and obtained both nuclear and side-chain nitration products. The only related prior report on t-butylbenzene is one by Konovalov,[15] who heated it with with dilute nitric acid under pressure, and obtained only a side-chain nitro-derivative.

In the course of our experiments by the vapour-flow method with t-butylbenzene and nitric acid, we did observe nuclear nitration, the main product of which was *p*-nitro-t-butylbenzene, but only under such conditions as to indicate that this product was being formed, not in the gas phase, but by ordinary electrophilic nitration, presumably by

[10] Seubold, *J. Amer. Chem. Soc.*, 1953, **75**, 2532.
[11] Urry and Kharasch, *J. Amer. Chem. Soc.*, 1944, **66**, 1438.
[12] Bullock and Mitchell, *J. Amer. Chem. Soc.*, 1941, **63**, 3230.
[13] Hass and Riley, *Chem. Rev.*, 1943, **32**, 383.
[14] Titov, *J. Gen. Chem. U.S.S.R.*, 1940, **62**, 1855.
[15] Konovalov, *Jahresber.*, 1895, p. 1538.

XUM

nitronium ion, in the liquid condensate formed by the gases emerging from the hot space. Thus nuclear nitration was observed if the nitric acid supplying the vapour feed were so concentrated, *e.g.*, 95%, that it would, as liquid, rapidly nitrate t-butylbenzene. Further, the extent of nuclear nitration in the products of vapour-flow experiments increased in proportion as, by keeping the vapour flow-rate up or the temperature of the hot space down, unchanged nitric acid and t-butylbenzene both emerged therefrom to be condensed together. Nuclear nitration was not observed when the nitric acid supplying the vapour feed was so dilute (68% or less) that it could not, as liquid, nitrate t-butylbenzene in the time available to the condensate; this remained true independently of the flow-rates and temperatures employed for the gas reaction. These results allow us to disregard Bullock and Mitchell's report of the gaseous nuclear nitration of toluene, for the nitric acid supplying their vapour feed was always of concentration above 70% and their hot space was at only 150°. Probably little happened until their materials, emerging from the hot space, were recondensed, when ordinary electrophilic substitution took place in the condensate.

We did not observe any nuclear nitration by nitrogen dioxide when t-butylbenzene was treated with it by the vapour-flow method, but we did observe it, with the production, particularly, of *p*-nitro-t-butylbenzene, during experiments in which liquid t-butylbenzene and dinitrogen tetroxide were heated together under pressure. However, we only then observed it in experiments in which a visible acid layer appeared, either before heating owing to insufficient care to exclude moisture when loading the tubes, or after heating because the nitration and oxidation had been allowed to go so far as to produce enough water to make a visible layer. In those experiments in which no acid layer was formed, no *p*-nitro-t-butylbenzene appeared. Since any formed acid layer must consist largely of nitric acid, it seems clear that nuclear nitration, when observed, results from ordinary electrophilic substitution presumably by nitronium ion, in an aqueous-acid phase. We therefore conclude that in Titov's experiments, in which toluene and dinitrogen tetroxide were heated together under pressure, the nitrotoluenes arose by nitration in an acid layer whose presence was not noticed.

In all the experiments now to be summarised on the gaseous nitration of t-butylbenzene, conditions were avoided in which the hydrocarbon could be nitrated by nitric acid in a liquid phase.

A large number of experiments in which the vapours of t-butylbenzene and aqueous nitric acid were injected to produce gas mixtures of the composition 0·5—2·0 mol. of hydrocarbon, plus 1 mol. of nitric acid, plus 1·65 mol. of water into a reaction space at temperatures from 200° to 350°, at rates allowing reaction times from many minutes at the lower temperatures to a few seconds at the upper, gave closely similar products. In all cases, apart from unchanged hydrocarbon recovered, the main product was ω-nitro-t-butylbenzene. The chief by-product was nitrobenzene. Next in order of importance came acetophenone and benzoic acid, then *o*-nitrophenol and 2,4-dinitrophenol. Acetic, oxalic, and formic acids and carbon dioxide were also isolated as such or as derivatives. Tars, and also traces of many unidentified chromatographically distinct products, were formed. A typical weight distribution of identified aromatic products, based on 100 g. of t-butylbenzene used but not recovered and assumed converted, was as follows: 48 g. of ω-nitro-t-butylbenzene, 17 g. of nitrobenzene, 14 g. of an acid fraction whose chief components were benzoic acid > *o*-nitrophenyl > 2,4-dinitrophenol, and 4 g. of acetophenone. About 12 g. of partly acidic and partly non-acidic tar were obtained. An assay of the identified aliphatic acids was not attempted.

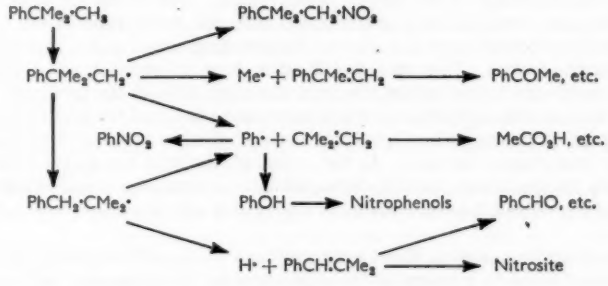
A further series of experiments was conducted in which t-butylbenzene vapour and nitrogen dioxide, in the proportions of 0·5—8·5 mol. of the former to 1 mol. of the latter, were injected into a reaction space at 325°, at a rate which allowed 30—40 sec. for the reaction. The identified products were as before, and in very similar proportions, together with unidentified chromatographically distinguishable traces of other products and tar, but with less of the latter than in the previous series of experiments.

None of these products has to be attributed to rearrangement in a 2-methyl-2-phenylpropyl radical, for none has either a hydrogen atom bound to the α-carbon atom, or a methyl group bound to the β-carbon atom of an aromatic side-chain. Now this might occur, either because the 2-methyl-2-phenylpropyl radical is never formed, or because it is, when formed, too closely surrounded by species eager to react with it to be allowed to survive the length of time required for its rearrangement. We therefore investigated the effect of considerable dilution of the reactants with water vapour. In contrast to liquid-phase nitration, in which water has a specific significance as a base and as a medium controlling the electrolytic situation, the rôle of water vapour in gas-phase nitration, as Bachman has concluded, is only the relatively non-specific one of a carrier gas.

Experiments were therefore conducted in which vapours of t-butylbenzene and dilute aqueous nitric acid, in proportions to produce gas mixtures of the composition 2—5 mol. of hydrocarbon plus 1 mol. of nitric acid plus 40—90 mol. of water, were supplied to the reaction space at 325—350°, with rates allowing reaction times of 10—40 sec. All the identified products previously mentioned were again obtained, and also benzaldehyde and ωω-dimethylstyrene nitrosite, both of which must have arisen from a rearrangement of the 2-methyl-2-phenylpropyl radical. It is possible that dimethylstyrene emerges as such from the hot space, and is converted into its nitrosite only in the condensate, for this conversion is very easily done by oxides of nitrogen at room temperature, a reaction that affords a convenient means of separating and characterising the hydrocarbon. Typical yields, per 100 g. of t-butylbenzene used but not recovered and assumed converted, were 40 g. of ω-nitro-t-butylbenzene, 12 g. of nitrobenzene, 28 g. of total aromatic acids, 5 g. of ωω-dimethylstyrene nitrosite, and 1·5 g. of benzaldehyde, along with other products.

With the identification of rearrangement products, our main aim was accomplished, for we could conclude that alkyl radicals certainly arise in gas-phase nitration.

The scheme set out below should be considered as no more than a plausible way of understanding the formation of the products. The assumption of the scheme is that the 2-methyl-2-phenylpropyl radical is first produced, that then it either combines with nitrogen dioxide, or is degraded to olefins, or rearranges, and that the rearranged radical is mainly degraded. Many variants of the scheme would be as plausible. For example, the only reason why we make no use of Bachman's idea that alkyl nitrites might be intermediates in oxidations is the inconclusive one that, whilst we were unable to prepare 2-methyl-2-phenylpropyl nitrite, we did make the nitrite of the rearranged radical, and found it to be thermally stable under the conditions of our nitrations.



Experimental

Preparations.—t-Butylbenzene, either fractionated commercial material, or prepared from benzene, t-butyl chloride, and ferric chloride, had b. p. 168·5—169°, n_D^{25} 1·4905.

Attempts were made to prepare and discover the properties of some of the products that might arise in the gas-phase nitration of t-butylbenzene. 1-Benzyl-1-methylethanol, b. p.

88·5—89°/7·0 mm., n_D^{25} 1·5138, prepared from benzylmagnesium chloride and acetone, was converted by hydrogen bromide into the bromide, b. p. 88—89°/5·3 mm., n_D^{25} 1·5382, and this was treated with silver nitrite to give the nitrite, b. p. 88—89°/7·5 mm., n_D^{25} 1·5139, which could be reduced with zinc and aqueous ammonium chloride to restore the alcohol (3,5-dinitrobenzoate, m. p. 97°). The nitrite on passage as vapour through the gaseous nitration tube with the hot space at 300° was unchanged. An attempt to make the isomeric nitro-compound by reaction between benzyl bromide and the sodium salt of 2-nitropropane failed, benzaldehyde and acetoxime being obtained. An attempt to prepare 2-methyl-2-phenylpropyl nitrite from the corresponding chloride and silver nitrite failed, because rearrangement occurred to give the isomeric nitrite. A by-product of this reaction was ωω-dimethylstyrene, which was prepared in larger amount, as described in the literature, by pyrolysis of 1-benzyl-1-methylethyl bromide, and, more conveniently, by refluxing 1-benzyl-1-methylethanol with a crystal of iodine for several hours. The hydrocarbon had b. p. 71—72°/13 mm., 78—79°/20 mm., n_D^{25} 1·5322; on treatment in ether with the gases from acetic acid–sodium nitrite, it at once gave crystals of its nitrosite which, crystallised from chloroform, had m. p. 116° (Found: C, 57·9; H, 5·93; N, 13·9. Calc. for $C_{10}H_{13}O_3N_3$: C, 57·7; H, 5·81; N, 13·5%). The isomeric hydrocarbon, 2-methyl-3-phenylprop-1-ene, prepared by pyrolysis of 2-methyl-2-phenylpropyl chloride, does not give a crystalline nitrosite in these conditions. From a cursory study, we gained the impression that pyrolysis of ω-nitro-t-butylbenzene too slow to be important in determining the products of the vapour-phase nitrations here described; it was ascertained that no nitrobenzenes arises in this way. The ω-nitro-compound had b. p. 127°/7 mm., n_D^{25} 1·5240, and was converted by aqueous sodium hydroxide into a crystalline sodium salt, from which it could be recovered by acidification. Hot alkaline permanganate oxidised it to α-phenylisobutyric acid, m. p. 77°, convertible through the chloride to the amide, m. p. 160—161°. In order to simplify characterisation, the ω-nitro-compound was nitrated with fuming nitric acid to p*ω-dinitro-t-butylbenzene*, which, crystallised from aqueous ethanol, had m. p. 64—65° (Found: C, 67·2; H, 7·5; N, 8·1. $C_{10}H_{12}O_4N_2$ requires C, 67·0; H, 7·3; N, 7·8%). *p*-Nitro-t-butylbenzene, prepared by nitration of *t*-butylbenzene with fuming nitric acid in the liquid phase, had b. p. 126°/7 mm., m. p. 28—29°, n_D^{25} 1·5300; it was insoluble in alkali. It was further characterised by conversion into *p*-acetamido-t-butylbenzene, m. p. 172—172·5°.

Apparatus.—Liquid t-butylbenzene was delivered from a constant-head burette, through an internally sealed nozzle, the drops from which could be counted, into the top of a vertical capillary tube, the rate of flow of liquid through which, and hence the dropping rate, could be adjusted by pushing a Nichrome wire into it. The capillary descended, made a U-turn, and immediately on the other side of this the rising tube was joined to a vertical length of wider tubing, which was surrounded by an electric furnace. This was the " vaporiser "; from it the vapour passed into the inner of two concentric horizontal tubes, which were surrounded by another electric furnace. This was the " preheater," in which the separate vapours were brought to the reaction temperature, before being mixed. The vapour of aqueous nitric acid was delivered through a second such arrangement into the outer tube of the preheater. In some experiments in which nitrogen dioxide was the nitrating agent, water vapour was delivered through this second system. The nitrogen dioxide was delivered from a glass container, through a screw-valve and a flow-meter, also into the outer tube of the preheater. Both tubes of the preheater were constricted just where the inner one ended, and the preheated gases became mixed, thus to pass on through the " reaction vessel," which was a 1-metre length of 2·5 cm. diam. tube in its own electric furnace. To the outlet of this tube was sealed a 15-cm. length of downward-sloping air-condenser, which delivered into a receiver, surmounted by a water-condenser, to the top of which solid-carbon-dioxide-cooled and liquid-air-cooled traps could be attached.

Method.—The dropping rates or flow-meter readings of the different delivery systems were calibrated for actual rate of a passage of the substances by trapping and weighing. Before an experiment, each delivery system used was set to deliver at the required rate. Then, the temperatures of the vaporisers, preheater, and reaction vessel having been set, and the collecting apparatus assembled, the delivery systems were connected to the preheater. The delivery rates were usually set on the basis of a preconceived delivery-rate ratio, and a reaction time which settled itself as a result of a preliminary experiment, as follows. The reactants were fed through in the required rate-ratio, but at individual rates which were gradually diminished together until brown fumes ceased to emerge from the reaction vessel. The rates of flow, the volume of

XUM

the vessel, and the temperature and pressure (atmospheric) being known, the period of time available for the gas reaction could be calculated.

Separation of Products.—Carbon dioxide was identified in the liquid-air-cooled trap. In the solid-carbon-dioxide-cooled trap, after evaporation of the nitric oxide an oily and an aqueous layer remained, from which non-volatile oxalic acid was isolated. The volatile components were added to the contents of the main receiver, where also there had collected an aqueous and an oily layer. The aqueous solution was basified, concentrated, acidified with sulphuric acid, and distilled, to give a first fraction of water and formic acid, in which the latter was identified as its *p*-bromophenacyl ester, m. p. and mixed m. p. 133—133·5°. The oily layer from the receiver was stripped of acids with aqueous sodium carbonate, when some tar separated; and the alkaline aqueous solution was acidified, and extracted with ether. The residue left on evaporation of the ether was distilled to give a first fraction consisting mainly of acetic acid, characterised as its *p*-bromophenacyl ester, m. p. and mixed m. p. 84—85°. The residue after removal of acetic acid was distilled in steam, to give a yellow oil followed by less coloured substances; all these materials were collected in ether and chromatographed on alumina. The lowest band was yellow; from it *o*-nitrophenol was eluted (m. p., mixed m. p., and benzoyl derivative). The next band was of benzoic acid (m. p. and mixed m. p.). The next one, rather firmly held, had to be washed out with sodium hydroxide as a red soluble salt, which, on acidification, gave 2,4-dinitrophenol (m. p., mixed m. p., and benzoyl derivative). The residue from the steam-distillation was similarly chromatographed, to yield 2,4-dinitrophenol, and a very elaborate chromatogram which, having no outstanding bands, was not further examined. The oily layer from which acids had been stripped was distilled under reduced pressure. The first distillate consisted of unchanged t-butylbenzene. As a routine, this material was extracted with sodium hydrogen sulphite solution before being redistilled, and the extract was examined for carbonyl compounds, though with no result, except as described later. After the hydrocarbon had passed over, there followed a combined fraction of acetophenone and nitrobenzene which, by redistillation, could be approximately separated. The former was identified as its 2,4-dinitrophenylhydrazone, and the latter by conversion into acetanilide and benzanilide. The main product, ω-nitro-t-butylbenzene, came over as the last distillable fraction, to leave a pitch-like residue. This fraction was usually collected at 126—129°/7 mm., and on redistillation had a sharper b. p., *e.g.*, 126·8—127·2°/7·1 mm. (Found: C, 67·2; H, 7·56; N, 8·1. Calc. for $C_{10}H_{13}O_2N$: C, 67·0; H, 7·31; N, 7·8%). It had to be carefully distinguished from isomers, *e.g.*, *p*-nitro-t-butylbenzene, which has almost the same b. p., and the unknown but conceivable 2-benzyl-2-nitropropane. That our ω-nitro-compound did not contain either of these isomers was shown by the fact that it was completely converted by aqueous sodium hydroxide into a white crystalline sodium salt, which, on extraction with ether, gave no product, unless it was first acidified, when it regenerated the original nitro-compound. Further confirmation of the identity of the nitro-compound was secured by oxidising it with hot alkaline permanganate to α-phenylisobutyric acid (cf. p. 2740), a product not obtainable by oxidation of any other isomer. For routine characterisation, the nitro-compound was converted by liquid-phase nitration with fuming nitric acid into *p*ω-dinitro-t-butylbenzene, m. p. 64—65° (cf. p. 2740).

In nitrations with vapour from highly aqueous nitric acid, two additional products appeared. First, crystals found in the main receiver were collected, preferably as soon as their separation appeared to be complete, as they slowly redissolved if left. This substance, crystallised from chloroform–ethanol, had m. p. 116° (Found: C, 56·0; H, 5·9; N, 13·8%). ωω-Dimethylstyrene nitrosite has been recorded as having m. p. 112° and 156°, but not 116°. However, made (cf. p. 2740) from authentic ωω-dimethylstyrene, it has m. p. 121°, and was identical with the substance from the vapour-phase nitration. The second additional substance was benzaldehyde. During the distillation of the non-acidic product, it came over mainly in the tail of the hydrocarbon fraction. It was extracted therefrom with aqueous sodium hydrogen sulphite, recovered, and converted into its 2,4-dinitrophenylhydrazone. All experiments which yielded ωω-dimethylstyrene nitrosite yielded benzaldehyde. If, through delay in the collection of the nitrosite crystals, the yield of that substance was lower than usual, then the yield of benzaldehyde was comparably higher, as if the former product became converted into the latter when left in the receiver with the other products of the vapour-phase nitration.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1.

[*Received, March 18th,* 1959.]

549. *Homolytic Substitution at a Saturated Carbon Atom. Part II.* Products of the Photoinduced Gaseous Chlorination of t-Butylbenzene.*

By J. D. Backhurst, E. D. Hughes, and Sir Christopher Ingold.

The test for intervention of alkyl radicals in aliphatic substitution, which uses t-butylbenzene as substrate, and relies on a formed 2-methyl-2-phenylpropyl (neophyl) radical to disclose itself by rearrangement, is verified by application to a reaction of known mechanism, namely, photoinduced chlorination in the gas phase. In theory, the test presupposes a radical life long enough to permit this activated rearrangement, and therefore it was for experimental determination whether it would be applicable to a mechanism providing only a short radical life, for example, a chain reaction, such as chlorination is known to be, of great chain length, where radical life is determined by the fast step of each unit process of chain-propagation. The rearrangement does occur in the gaseous chlorination of t-butylbenzene.

It is assumed that kinetics are not useful for exploring mechanism in the present studies of homolytic substitution, though they may later be for confirmation, and that the piecemeal establishment of single points of mechanism by *ad hoc* tests holds better prospects. In Part I, one such test, that for the intervention of free alkyl radicals, was successfully applied to a reaction of unknown mechanism, aliphatic nitration, but the validity of the test required to be checked by application to a reaction of known mechanism: chlorination was used.

As before, we took t-butylbenzene as substrate, so that the alkyl radical, if formed, would be 2-methyl-2-phenylpropyl (neophyl), which, uniquely among such simple radicals, would, in the length of life it has in some reactions, isomerise to give products which establish its intervention.[1] A certain length of life had to be provided, because rearrangement of the radical is somewhat slow, having an estimated activation energy of at least 8 kcal./mole.[2] Our problem was therefore to find out whether the 2-methyl-2-phenylpropyl radical, if an intermediate in a homolytic substitution, particularly one having a chain mechanism of numerous very rapid steps, would survive long enough to isomerise. In order to allow it a maximal opportunity so to do, we worked in the gas phase, and were prepared to go to low partial pressures.

The prototype of homolytic chlorination is the chlorine–hydrogen reaction, for which, on the basis of experiments by Bodenstein and others, Nernst proposed the first specific chain mechanism,[3] which all subsequent work has confirmed [4] (R = H):

$$Cl + HR \longrightarrow HCl + R;\ R + Cl_2 \longrightarrow RCl + Cl$$

The chlorination of alkanes, whether thermally [5] or photochemically [6] induced, shows just the same kinetic characteristics, and must have an identical mechanism [7] (R = alkyl). Chain-lengths are commonly 10^4—10^6. The first step (above) is rate-controlling, but is nevertheless very fast, having the activation energy 3·85 kcal./mole for methane, and lower values for other hydrocarbons.[8] The second step, which determines the life of the radical R, follows the first so very quickly that the first is not detectably reversed.

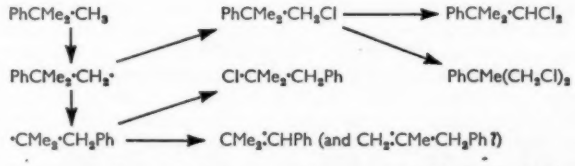
* Part I, preceding paper.

[1] Urry and Kharasch, *J. Amer. Chem. Soc.*, 1944, **66**, 1438.
[2] Seubold, *J. Amer. Chem. Soc.*, 1953, **75**, 2532.
[3] Nernst, *Z. Elektrochem.*, 1918, **24**, 335.
[4] Hinshelwood, "Kinetics of Chemical Change in Gaseous Systems," Clarendon Press, Oxford, 1933, p. 100; Semenoff, "Chemical Kinetics and Chain Reactions," Clarendon Press, Oxford, 1935, p. 89.
[5] Pease and Walz, *J. Amer. Chem. Soc.*, 1931, **53**, 3728.
[6] Coehn and Cordes, *Z. phys. Chem.*, 1930, **89**, 1; Jones and Bates, *J. Amer. Chem. Soc.*, 1934, **56**, 2282; Tamura, *Rev. Phys. Chem. Japan*, 1941, **15**, 86; Ritchie and Winning, *J.*, 1950, 3579.
[7] Semenoff, ref. 4, p. 122; Steacie, "Atomic and Free Radical Reactions," Reinhold Publishing Corp., New York, 1954, p. 667; Walling, "Free Radicals in Solution," John Wiley and Sons Inc., New York, 1957, p. 352.
[8] Pritchard, Pyke, and Trotman-Dickinson, *J. Amer. Chem. Soc.*, 1955, **77**, 2629.

XUM

Unlike aliphatic nitration, aliphatic chlorination is not accompanied by degradation. Hass, McBee, and Weber have concluded [9] that, like nitration, chlorination is free from skeletal rearrangements, and also that every possible monochlorination product is always formed, the rates of hydrogen replacement, which are in the order tertiary > secondary > primary at lower temperatures, tending towards equality at higher. These general principles are confirmed in Walling's more recent and extensive collation [10] of data on relative rates and products of aliphatic chlorination.

In our experiments, preheated t-butylbenzene vapour and chlorine, in ratios between 3 : 1 and 10 : 1, were passed at atmospheric pressure, and at rates giving reaction times between 5 and 60 sec., through a Pyrex tube at some uniform temperature between 190° and 245°, and illuminated by mercury arcs. No clear difference of result was caused by packing the reaction tube with narrow tubes in order to increase 4-fold the surface area. The condensed product was fractionated, and, from the distillation graph, its composition was determined. The losses on distillation were usually not much more than 1%. Six products were identified, unchanged t-butylbenzene (283·5 g.), ωω-dimethylstyrene (2·0 g.), 1-benzyl-1-methylethyl chloride (14·3 g.), 2-methyl-2-phenylpropyl chloride (69·0 g.), ωω-dichloro-t-butylbenzene (5·0 g.), ωω′-dichloro-t-butylbenzene (4·0 g.). The yields shown are fairly typical, except that ωω-dimethylstyrene was not obtained from experiments at the lower temperatures. 2-Methyl-2-phenylpropyl chloride was always the main product, and 1-benzyl-1-methylethyl chloride was nearly always second in importance. The latter isomer is the chloride of the rearranged radical. ωω-Dimethylstyrene is a dehydrogenation product of the rearranged radical. 2-Methyl-2-phenylpropyl chloride underwent no conversion into 1-benzyl-1-methylethyl chloride under the conditions of production of these substances. However, the two dichlorides could be produced together by chlorination of 2-methyl-2-phenylpropyl chloride under similar conditions, and we therefore assume that they were produced from t-butylbenzene by way of this chloride. The following conversion scheme is, of course, partly hypothetical:



These experiments confirm what was certain from the kinetics of alkane chlorinations, namely, that the 2-methyl-2-phenylpropyl radical intervenes in the gaseous chlorination of t-butylbenzene. They show also, however, that the radical intervenes with a free life long enough to permit rearrangement, notwithstanding that the reaction involves long kinetic chains, in which even the slower propagation step is very fast, and radical life is determined by the faster propagation step. This conclusion justifies our using t-butylbenzene as a test for the intervention of alkyl radicals in aliphatic substitutions of unknown mechanism, as already illustrated in Part I with respect to nitration.

Experimental

Materials.—t-Butylbenzene, from benzene, t-butyl chloride, and ferric chloride, had b. p. 51°/10 mm., n_D^{25} 1·4905. 2-Methyl-2-phenylpropyl chloride, from benzene and 2-methylallyl chloride,[11] had b. p. 94—95°/9 mm., n_D^{25} 1·5227. It was characterised by nitration (fuming HNO_3) to its *p*-nitro-derivative, b. p. 142—143°/1·4 mm., m. p. 54°, which was reduced (Sn–HCl) to an amine whose acetyl derivative had m. p. 154°. 1-Benzyl-1-methylethyl chloride, from

[9] Hass, McBee, and Weber, *Ind. Eng. Chem.*, 1935, **27**, 1190; 1936, **28**, 333.
[10] Walling, ref. 7, p. 356.
[11] Smith and Sellas, "Organic Syntheses," 1952, **32**, 90.

the alcohol (Part I), hydrogen chloride, and zinc chloride, had b. p. 85°/10 mm., n_D^{25} 1·5132. It was characterised by conversion, by treatment of its Grignard compound with phenyl isocyanate, into benzyldimethylacetanilide, m. p. 107·5°. ωω-Dimethylstyrene and its nitrosite are described in Part I.

Apparatus.—The system for supplying the reaction vessel with t-butylbenzene vapour at known flow-rate and temperature was as described in Part I. This vapour passed through the outer tube of the preheater; chlorine from a cylinder, dried ($CaCl_2$) and flow-metered, was passed along the inner tube. The chlorine was metered with a rotameter, consisting of a vertical tapered tube, up which it passed, lifting a Koramite float whose equilibrium position gave the rate of passage. A constriction in the outer tube of the preheater prevented back-diffusion. The outlet of the inner tube was so constructed that the outflow of chlorine was radial to the flow of hydrocarbon, thus ensuring efficient mixing in the reaction vessel, a 95 cm. length of Pyrex tube, 2·5 cm. in diameter, with an external heater winding surrounded by another Pyrex tube for thermal protection. Two mercury-discharge lamps, 15 cm. above the reaction vessel, provided the required irradiation, which was screened from the preheater, from the region of mixing of the gases, and from the condensing and collecting arrangements. The latter were similar to those described in Part I, except that strongly cooled traps proved unnecessary.

Method.—The required temperatures having been established, the apparatus was swept with oxygen-free nitrogen. The chlorine supply system was detached at the outlet end of the flow-meter, swept with chlorine, and reconnected. Meanwhile, the hydrocarbon supply system was started and regulated. When the hydrocarbon, having displaced the nitrogen in the preheater and reaction vessel, could be seen condensing, the chlorine supply was started and regulated. After a period sufficient for the attainment of steady conditions, the irradiation was started, and, after a further such period, the metering of supplies and collection of products were begun. At the end of the reaction period the apparatus was swept with nitrogen, which was also passed through the liquid condensate to carry off hydrogen chloride.

Separation of Products.—They were separated by distillation, under reduced but regulated pressure, with a long vacuum-jacketed column operating at high reflux ratio. Boiling points and refractive indices for one experiment are in the Table. Both sets of constants allow distillation curves to be constructed, which show the six components and provide a basis for their estimation.

Distillation results (*Run* 21).

Hydrocarbon : chlorine ratio 4·2; temp. 240°; time 29 sec.

Fract. No.	B. p. (10·0 mm.)	Wt. (g.)	n_D^{25}	Fract. No.	B. p. (10·0 mm.)	Wt. (g.)	n_D^{25}
1	50·0—51·0	195·1	1·4905	13	88·7—90·0	2·9	1·5155
2	50·0—51·0	82·3	1·4905	14	90·0—93·0	1·9	1·5172
3	51·0—52·0	4·3	1·4910	15	93·0—94·7	1·2	1·5202
4	52·0—60·0	3·2	1·4910	16	94·7—96·5	34·9	1·5228
5	60·0—65·0	0·6	1·5122	17	96·5	20·2	1·5228
6	67·8—69·2	1·0	1·5263	18	95·0	13·1	1·5230
7	69·2—72·0	0·8	1·5283	19	95·0—90·0	3·3	1·5243
8	72·0—81·0	0·7	1·5234		(4·0 mm.)		
9	81·0—86·0	1·8	1·5200	20	72·0—90·0	0·8	1·5343
10	86·0—87·3	2·4	1·5150	21	90·0—95·0	3·7	1·5378
11	87·3—87·0	1·8	1·5150	22	98·0—100·0	3·1	1·5465
12	87·0—88·7	2·4	1·5153	23	100·0—101·0	0·7	1·5482

Fractions 1—3 consisted of t-butylbenzene. Fraction 5 was unsaturated and had the odour of 2-benzylpropene; but this hydrocarbon, which we prepared, is not easy to characterise (*e.g.*, it seems not to form a crystalline nitrosite), and we were not able to confirm its presence here. Fraction 7 marks a sharp peak in the refractive-index curve of the distillate, and was identified as ωω-dimethylstyrene (Found: C, 91·0; H, 9·4. Calc. for $C_{10}H_{12}$: C, 90·9; H, 9·1%), by conversion into its nitrosite, m. p. 116° (Part I). Fractions 6 and 7, in combination with similar material from other experiments, when redistilled, gave material of b. p. 68°/10 mm., n_D^{25} 1·5350—1·5370. Fraction 11 was characterised as 1-benzyl-1-methylethyl chloride (Found: C, 71·5; H, 7·9; Cl, 20·9. Calc. for $C_{10}H_{13}Cl$: C, 71·2; H, 7·8; Cl, 21·0%) by conversion into benzyldimethylacetanilide, m. p. 107·5°. Fractions 10—13, on redistillation,

XUM

gave material of b. p. 85°/10 mm., n_D^{25} 1·5135. Fraction 17 was identified as 2-methyl-2-phenylpropyl chloride (Found: C, 71·5; H, 8·0; Cl, 21·2%) by conversion into 2-*p*-acetanilido-2-methylpropyl chloride, m. p. 154°. Fraction 21, on redistillation, gave a material of b. p. 98°/4·0 mm., n_D^{25} 1·5387, which was identified as 1,1-*dichloro-2-methyl-2-phenylpropane* (Found: C, 59·5; H, 6·1; Cl, 34·9. $C_{10}H_{12}Cl_2$ requires C, 59·1; H, 6·0; Cl, 34·9%) by comparison of its infrared spectrum with that of the same substance, prepared as described below. Fractions 22 and 23 on redistillation yielded a sample of b. p. 115°/4 mm., n_D^{25} 1·5475, which was identified as 1,3-*dichloro-2-methyl-2-phenylpropane* (Found: C, 58·9; H, 5·9; Cl, 35·6%) from its infrared spectrum (see below).

Chlorination of 2-Methyl-2-phenylpropyl Chloride.—For production of the two dichlorides on a preparative scale, 2-methyl-2-phenylpropyl chloride (300 g.), refluxing under 120 mm., and later under 150 mm., was treated with a stream of chlorine under irradiation from mercury arcs. A preliminary fractionation of the product through a short column gave a first fraction of unchanged chloride (77 g.), a fraction of b. p. 98—110°/4·0 mm. and n_D^{25} 1·536—1·542 (95 g.), and a fraction of b. p. 110—120°/4·0 mm. and n_D^{25} 1·545—1·552 (95 g.). The second of these fractions, on redistillation through a long vacuum-jacketed column at high reflux ratio, gave a compound (75 g.) of b. p. 98°/4·0 mm. and n_D^{25} 1·5376 (Found: C, 59·0; H, 6·0; Cl, 34·6%). The third, on similar treatment, gave a compound (55 g.) of b. p. 113°/4·0 mm. and n_D^{25} 1·5473. These two substances were identical (infrared spectra) with 1,1- and 1,3-dichloro-2-methyl-2-phenylpropane of the preceding paragraph.

1,1-*Dichloro-2-methyl-2-phenylpropane.*—2-Methylallyl chloride was isomerised by stirring with 80% sulphuric acid at 40° for 2·5 hr. to 2,2-dimethylvinyl chloride, b. p. 66—68°, which, on chlorination by chlorine at 0° in presence of excess of sodium hydrogen carbonate, was converted into 2-methylallylidene chloride, b. p. 108—112°, n_D^{25} 1·4550.[12] Following the method of conversion of 2-methylallyl chloride into 2-methyl-2-phenylpropyl chloride,[11] 2-methylallylidene chloride (0·18 mol.) was stirred with benzene (0·5 mol.) and sulphuric acid (2·0 ml.) for 30 hr. at 15°. The product, on fractionation, gave a material (1·25 g.) of b. p. 78°/0·7 mm., n_D^{25} 1·5350, which had infrared bands at 707, 724, 752, 775, 824, 858, 886, 939, 1052, 1100, 1110, and 1220 cm.$^{-1}$, identical in form and position with those of the above samples of 1,1-dichloro-2-methyl-2-phenylpropane.

1,3-*Dichloro-2-methyl-2-phenylpropane.*—It was necessary first to prepare 3-chloro-2-chloromethylprop-1-ene. Mooradian and Cloke's route [13] from pentaerythritol, through its trichlorohydrin, to the oxidation product of the latter, tris(chloromethyl)acetic acid, which should, by their account, have been easily decarboxylated and dehydrochlorinated with quinoline, was unsuccessful. We also tried the addition of hypochlorous acid to 2-methylallyl chloride, expecting to dehydrate the formed 1,3-dichloro-2-methylpropan-2-ol with sulphuric acid, phosphoric acid, or iodine; again, we tried chlorination of 2-methylallyl chloride by passing chlorine into the refluxing material, so obtaining a fraction of b. p. 135—140° as well as the expected 1,2,3-trichloro-2-methylpropane, b. p. 162—170°, which we attempted to dehydrochlorinate with quinoline. We were unable to develop well any of these processes, but almost all attempts gave some material boiling in the range 130—140°. As 1,3-dichloro-2-methylprop-1-ene is recorded [14] as having b. p. 132°, and 3-chloro-2-chloromethylpropene, b. p. 138°, we assumed this fraction to be a mixture of the two; as either isomer should give the required product in reaction with benzene, we used the whole fraction for this purpose. It was stirred with benzene and sulphuric acid, as in the similar preparation in the preceding paragraph. The product, on fractionation, gave a material (0·75 g.) of b. p. 116°/4 mm., n_D^{25} 1·5484, which had infrared bands at 717, 745, 766, 830, 872, 908, and 1001 cm.$^{-1}$, identical in form and position with those of the two already described samples of 1,3-dichloro-2-methyl-2-phenylpropane.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER ST., LONDON, W.C.1. [*Received, March 18th*, 1959.]

[12] Huntress, "Organic Chlorine Compounds," John Wiley and Sons, Inc., New York, 1948, p. 1042.
[13] Mooradian and Cloke, *J. Amer. Chem. Soc.*, 1945, **67**, 942.
[14] Huntress, ref. 12, pp. 727 and 732.

XUM

550. *The Constitution of Suint. Part II.* Organic Acids.*

By K. R. Deane and E. V. Truter.

The following acids have been identified in suint: acetic, propionic, n-butyric, n-valeric, oxalic, succinic, and glutaric. Paper chromatography indicated the presence of adipic and pimelic acid.

Suint is that portion of the sheep's fleece that is soluble in cold water after the wax has been removed. Older work shows that it is a complex mixture of metallic ions, organic acids, peptides, weak bases, neutral substances, and inorganic cations. A total of 41 organic compounds has been said to be present in the aqueous extract of raw wool (for a review see Truter [1]). Unfortunately, in no case has identification been adequate experimentally. In the older work (before 1955) no experimental measurements have been adduced; in recent studies by Farnworth [2] and by Green and Preston [3] the evidence is entirely chromatographic. Such evidence is unconvincing because it is becoming increasingly clear that in complex mixtures of closely related substances chromatographic measurements alone do not permit unequivocal identification. For example, the behaviour of the peptides in suint very closely resembles that of amino-acids; [4] further, in the present study it was found that the lower normal and iso-acids could not be distinguished by partition chromatography. Hence, chromatographic evidence *alone* does not *prove* the presence of a compound.

In the present study, suint from Australian merino wool has been fractionated by means of ion-exchange resins, into four main fractions: inorganic cations 44%; organic acids and anions 36%; weak bases 4%; and ampholytes 3%. Complete recovery may not always be achieved with ion-exchange resins, but here the discrepancy is large enough to suggest the presence of the ammonium ion, and of water-insoluble fatty acids which were originally present as water-soluble potassium salts. Farnworth,[2] in a detailed analysis of the inorganic cations, has found K, Na, Ca, Mg, Al, and Fe, and we have shown that the ampholyte fraction contains at least eleven peptides each of which contains between eight and thirteen different amino-acids.[4]

The steam-volatile organic acids (2%) were separated from one another by partition chromatography on silica, and on a larger scale by countercurrent distribution between carbon tetrachloride and dilute aqueous alkali. The presence of acetic, propionic, n-butyric, and n-valeric acid has been confirmed by preparation of their *p*-bromophenacyl esters. Contrary to expectation, because most of the acids of wool wax are of the branched-chain type, there are no branched-chain acids in suint. The acids not volatile in steam and also insoluble in ether (18%) are dibasic, ranging from oxalic to pimelic but excluding malonic acid. Of these, succinic and glutaric acid were identified as their *p*-phenylazoanils, and oxalic acid was identified by Martin's method.[5] The presence of adipic and pimelic acid is less certain, but was indicated by paper chromatograms.

A small amount of material was precipitated as 2,4-dinitrophenylhydrazone; this was not investigated. It may be derived from the keto-acids suggested by Green and Preston.[3] No steroids could be detected by the Liebermann–Burchardt reaction.

The approximate amounts of the acids recovered from suint were: acetic, 1·1%; propionic 0·2%; n-butyric 0·3%; n-valeric 0·2%; oxalic 0·3%; succinic 10%; and glutaric acid 1%. Each of these was pure by chromatographic standards.

* Part I, *Biochim. Biophys. Acta*, 1955, **18**, 435.

[1] Truter, "Wool Wax," Cleaver-Hume Press, London, 1956, pp. 61—72.
[2] Farnworth, *Austral. J. Appl. Sci.*, 1956, **7**, 233.
[3] Green and Preston, *J. Textile Inst.*, 1956, **47**, T497.
[4] Deane and Truter, *Biochim. Biophys. Acta*, 1955, **18**, 435.
[5] Martin, *Chem. and Ind.*, 1955, 427.

XUM

Experimental

Preparation of Suint.—Australian merino wool of 64's quality was sorted to remove gross impurities such as vegetable matter, and treated with light petroleum (b. p. 60—80°) in a Soxhlet apparatus for 8 hr. After removal of the solvent from the wool, the latter was gently squeezed in cold water (4 × 300 ml. per 100 g.). The aqueous solutions were combined and centrifuged until clear, and the concentration of solute was determined by evaporation of aliquot parts.

A suint solution (10·1 g./900 ml.) was passed through a column containing 550 c.c. of Zeo-Karb 225 in the H^+ form, at a rate of 18 ml./hr. The effluent contained anions, organic acids, and neutral substances (total 3·6 g.). The column was then washed with 2N-ammonia (1 l.), and the eluate, which contained weak bases and ampholytes, was concentrated to 500 ml. and passed through a column containing 250 c.c. of Deacidite FF in the OH^- form. The effluent from the second column contained only weak bases (0·4 g.). Further washing of the Deacidite FF column with N-hydrochloric acid (350 ml.) yielded the ampholytes (0·3 g.). Subsequently, treatment of the Zeo-Karb 225 column with N-hydrochloric acid (550 ml.) afforded a mixture of ammonium chloride (18·2 g.) and the cation chlorides (8·5 g.; equiv. to 4·4 g. of cations if the composition is assumed to be similar to that found by Farnworth).

Steam-volatile Acids.—The aqueous solution was adjusted to pH 2 with N-sulphuric acid. After the small amount of precipitate that was formed had been filtered off with a filter aid, the filtrate was treated with ether in a liquid–liquid extractor for 72 hr. The dried precipitate was also extracted with ether, and the combined ethereal extracts yielded a brown, sticky residue (3·0 g., 34·5%). The ether-soluble acids were extracted, as above, from a large amount of suint (32·9 g.) and distilled in steam. Titration of the distillate against ethanolic potassium hydroxide indicated that it contained 0·009 equivalent (*i.e.*, 0·27 mequiv./g.).

The volatile acids were examined on columns of silica which had been prepared according to Nijkamp's method.[6] Silica prepared by Sanger's method [7] was unsuitable.

Preparation of the Silica.—Commercial water-glass (*d* 1·35; 200 ml.) was mixed with water (400 ml.), acidified to Methyl Orange with 10N-hydrochloric acid, and stirred for 15 min. The resulting paste was ground with just sufficient 10N-hydrochloric acid to render it acidic to Thymol Blue, transferred to a Buchner funnel, and washed with water (about 4 l.) until free from chloride, without the filter-cake being allowed to become dry. The product was then set aside in 2% hydrochloric acid for 15 hr. and again washed free from chloride. Most of the water was removed by washing the filter-cake with 96% ethanol (about 1 l.), and the residue was dried at 80° for 18 hr. and then to constant weight at 150°.

Preparation of Columns.—Silica (0·6 g.) was mixed with a 0·8% solution of Bromocresol Green in dry methanol (0·12 ml.), and water (0·48 ml.) and 0·1N sodium hydroxide (0·3 ml.) were added. The apparently dry, blue-green product was mixed with carbon tetrachloride containing 6% of butan-1-ol, and the smooth slurry was transferred to a tube 270 × 7 mm. to give a column 6 cm. high. Preliminary experiments showed that a mixture of 0·01 milli-equivalent of each of the acids acetic, propionic, n-butyric, n-valeric, and hexanoic, could be separated on a 6 cm. column with an efficiency of 97%. Each acid, visible as a yellow band, was eluted and titrated, in an atmosphere of nitrogen, against 0·005N-sodium ethoxide with Cresol Red as indicator.

Potassium salts of the steam-volatile acids (190 mg.) were mixed with finely powdered Zeo-Karb 225 (500 mg.) in the H^+ form. Iso-octane (5 ml.) was added, and after the mixture had been shaken for 10 min. the mixture was centrifuged and the solvent decanted. The resin was washed with more iso-octane (3 × 5 ml.), and the combined washings were made up to 25 ml. Aliquot parts (1 ml.) of the solution were then chromatographed on silica (600 mg.) columns. Four clear bands were obtained, and the amounts of each, calculated on the dry suint, were: valeric (fastest band) 0·2%; butyric 0·3%; propionic 0·2%; and acetic acid 1·1%. Confirmatory evidence was obtained by collecting the acid from each band separately, mixing it with the appropriate known acid, and re-chromatographing the binary mixtures. In every case only a single band was observed, but the technique failed to separate the n-acids from the corresponding iso-acids. Hexanoic acid was absent.

Countercurrent Separation of the Volatile Acids.—The steam-volatile acids (5·2 milliequivs.) were subjected to thirty transfers in a countercurrent apparatus, with carbon tetrachloride

[6] Nijkamp, *Analyt. Chim. Acta*, 1951, **5**, 325; 1954, **10**, 448.
[7] Sanger, *Biochem. J.*, 1945, **39**, 507.

XUM

(50 ml.) and aqueous sodium hydroxide (0·1N; 50 ml.) as the solvents. Titration of the lower phases showed that the acids had separated into four distinct groups containing a total of 0·43 milliequiv. of acid. Correspondingly, the upper phases were combined into four fractions and the free acids which were liberated by treatment with Zeo-Karb 225 were titrated against 0·1N-alkali.

Fraction 1. n-Valeric acid, 0·81 milliequiv. Its *p*-bromophenacyl ester had m. p. and mixed m. p. 75° (Found: C, 52·3; H, 5·2. Calc. for $C_{13}H_{15}O_3Br$: C, 52·2; H, 5·1%). The isovaleric ester has m. p. 66° and when mixed with the derivative from suint the m. p. was 48—51°.

Fraction 2. n-Butyric acid, 0·33 milliequiv. Its *p*-bromophenacyl ester had m. p. and mixed m. p. 63° [mixed m. p. with the isobutyric ester (m. p. 77°) 54—58°] (Found: C, 50·4; H, 4·4; Br, 28·0. Calc. for $C_{12}H_{13}O_3Br$: C, 50·5; H, 4·6; Br, 28·0%).

Fraction 3. Propionic acid, 0·4 milliequiv. Its *p*-bromophenacyl ester had m. p. 63° (lit., m. p. 63°) (Found: C, 48·5; H, 4·4; Br, 29·2. Calc. for $C_{11}H_{11}O_3Br$: C, 48·7; H, 4·1; Br, 29·5%).

Fraction 4. Acetic acid, 2·5 milliequiv. Its *p*-bromophenacyl ester had m. p. 84° (lit., m. p. 85°) (Found: C, 47·4; H, 3·8. Calc. for $C_{10}H_9O_3Br$: C, 46·7; H, 3·5%).

Succinic Acid.—The acids not volatile in steam (33% of the suint) were treated with ether, and the yellow residue (18%) was decolorised with charcoal. Sublimation of the product under reduced pressure afforded needles, m. p. (sealed tube) 181° (12%) [Found: Equiv., 56·5. *M* (in camphor; extrapolation to zero concentration), 114]. After re-sublimation it had m. p. and mixed m. p. 185° (Found: C, 40·9; H, 5·3. Calc. for $C_4H_6O_4$: C, 40·7; H, 5·1%; *M*, 118; equiv., 59). Its *p*-bromophenacyl ester had m. p. and mixed m. p. 214·5—215° (Found: Br, 30·5. Calc. for $C_{20}H_{16}O_6Br_2$: Br, 31·2%). Paper chromatograms of succinic acid and the acid from suint had identical R_f values and a mixture gave only one spot, in the following solvents: (i) ethanol–aqueous ammonia (*d* 0·88)–water, 8 : 1 : 1 (Brown [8]); (ii) propan-2-ol–t-butanol–benzyl alcohol–water–90% formic acid, 1 : 1 : 3 : 1 : 2 (Stark *et al.*[9]); (iii) phenol–water, 3 : 1, containing 1% of 90% formic acid (Stark *et al.*[9]); (iv) tetrahydrofuran–3N-ammonia, 4 : 1 (Kalbe [10]).

Glutaric Acid.—The ether-insoluble acids which were not volatile in steam (230 mg.) were converted into their anhydrides by heating them with acetic anhydride (2 ml.). After the excess of acetic anhydride had been distilled off, the residue was heated in chloroform (2 ml.) with *p*-aminoazobenzene (300 mg.) in chloroform (2 ml.). When the mixture cooled, the anilic acids were precipitated; these were filtered off and heated under reflux with acetyl chloride (2 ml.) for 1 hr. to bring about cyclisation of the succinyl- and glutaryl-derivatives. Removal of the solvent gave a dark red solid (271 mg.). Part of this material (102 mg.) was placed on an alumina column (Spence type H; 100 × 1·4 cm.) and developed with benzene–ether (3 : 1). Three yellow bands were collected separately and a red band, possibly the anilic acids of homologous dibasic acids, remained on top of the column. Fraction 1: glutaro-*p*-phenylazoanil (5·3 mg.), m. p. and mixed m. p. 225° (Found: C, 69·1; H, 5·2. Calc. for $C_{17}H_{15}O_2N_3$: C, 69·6; H, 5·2%). Fraction 2: succino-*p*-phenylazoanil (81 mg.), m. p. and mixed m. p. 219° (Found: C, 68·7; H, 4·7. Calc. for $C_{16}H_{13}O_2N_3$: C, 68·8; H, 4·7%). Fraction 3: *p*-acetamidoazobenzene, m. p. 144°.

Other Dibasic Acids.—Hyflo-Supercel (40 g.) was washed with ether and with water, dried at 105°, mixed with 0·05N-sulphuric acid (28 ml.) and packed into a column (60 × 1·7 cm.) as a benzene slurry. The non-volatile acids of suint (466 mg.) were applied to the column and washed successively with benzene (200 ml.), ether (800 ml.) and butan-1-ol (600 ml.). The effluent was automatically collected as 10 ml. fractions, and each was titrated against 0·05N-sodium ethoxide. A group of six distinct, but incompletely separated fractions, followed by a seventh well-defined fraction, was obtained, but the recovery was only 86%. The first peak (approx. 15% of suint) contains higher aliphatic acids, and the next five peaks contain hydroxy-acids. It was expected that the dibasic acids would be eluted with butanol in the seventh fraction, so this material was chromatographed on paper after regeneration of the free acids by treatment of the sodium salts with Zeo-Karb 225. One-dimensional chromatograms in two solvents, (*a*) tetrahydrofuran–3N-ammonia, 4 : 1 (Kalbe [10]), and (*b*) propan-2-ol–t-butanol–benzyl alcohol–water, 1 : 1 : 3 : 1, containing 1% of 90% formic acids (Stark *et al.*[9]), indicated

[8] Brown, *Nature*, 1951, **167**, 441.
[9] Stark, Goodban, and Omen, *Analyt. Chem.*, 1951, **23**, 413.
[10] Kalbe, *Z. physiol. Chem.*, 1954, **297**, 19.

the presence of oxalic, succinic, glutaric, adipic, and pimelic acid. Malonic acid was not found.

Oxalic Acid.—The presence of oxalic acid was confirmed by Martin's specific test. The paper was sprayed with 10% aqueous potassium ferrocyanide, dried in the oven, and then sprayed with 0·5% ferric ammonium sulphate followed by ammoniacal ethanol. Oxalic acid was shown to be present by the development of a bright blue colour.

After, but not before, reduction of the non-volatile acids with magnesium and dilute sulphuric acid, followed by treatment with warm 2,7-dihydroxynaphthalene in concentrated sulphuric acid, a purple solution was obtained, indicating the presence of glycollic acid. This could be derived from oxalic or glyoxylic acid by reduction. Because only a trace of 2,4-dinitrophenylhydrazone could be obtained, it must be inferred that glyoxylic acid is not an important constituent, and that the colour reaction is due to the presence of oxalic acid.

The authors thank Professor J. B. Speakman for his interest in this work, and the International Wool Secretariat for financial assistance.

TEXTILE CHEMISTRY LABORATORY,
UNIVERSITY, LEEDS, 2.

[*Received, April 2nd,* 1959.]

---

551. *Reaction of Thiosulphate Ion with Tetraethylthiuram Disulphide promoted by Some Metal Cations.*

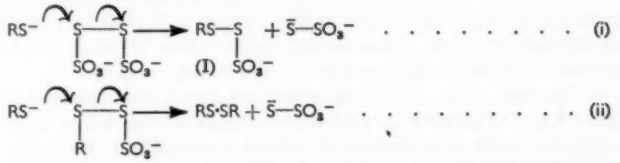
By B. SAVILLE.

Dialkyldithiocarbamate ions react readily with tetrathionate ions to give an almost quantitative yield of tetra-alkylthiuram disulphide and thiosulphate ions. The above reaction does not occur, however, when the zinc salt of diethyldithiocarbamic acid is used. This suggests that the above reaction products would react in the presence of zinc ions to give zinc dialkyldithiocarbamate and tetrathionate ions, a prediction now confirmed experimentally. Other metal cations such as Cd^{2+} and Pb^{2+} capable of yielding chelated salts with dialkyldithiocarbamic acids act similarly. Tentative mechanistic interpretations of these reactions are suggested.

THE use of tetrathionate ion as a reagent for the oxidation of thiols or thiol-acids, ionised in the presence of an added base, to the corresponding disulphidic species was introduced by Footner and Smiles,[1] and subsequently studied by Cambron and Whitby [2] and by Bulmer and Mann.[3] This reaction, which normally proceeds very rapidly in aqueous solution at room temperature, may be plausibly interpreted in terms of two successive thiol–disulphide interchange processes symbolised thus: (*a*) thiol ionisation in presence of base (B)

$$RSH + B \rightleftharpoons RS^- + BH^+$$

(*b*) reaction of thiol anion (RS^-) with tetrathionate ion



Since intermediates such as (I) have not been observed,* and since the disulphide (RS·SR)

* It has been claimed recently (Szczepkowski, *Nature*, 1958, **182**, 934) that cysteine and tetrathionate give "cysteine polythiosulphonic acids," an observation which is difficult to reconcile with the proposition made here. No idea of the proportions of these products is, however, indicated by these experiments.

[1] Footner and Smiles, *J.*, 1925, 2887.
[2] Cambron and Whitby, *Canad. J. Res.*, 1930, **2**, 144.
[3] Bulmer and Mann, *J.*, 1945, 674.

is obtained in nearly quantitative yield, it is concluded that process (ii) is much more rapid than process (i).

Although the above reactions are, in principle, reversible, there is no evidence from studies reported here that this reversal takes place to any significant extent. For example, an initially homogeneous system containing sodium thiosulphate and a tetra-alkylthiuram disulphide gave no tetrathionate and dialkyldithiocarbamate ions as required by reaction (iii):

$$2S_2O_3^{2-} + R_2N{\cdot}C(S){\cdot}S{\cdot}S{\cdot}C(S){\cdot}NR_2 \underset{\text{(iv)}}{\overset{\text{(iii)}}{\rightleftharpoons}} S_4O_6^{2-} + 2R_2N{\cdot}CS_2^-$$

Indeed, the reverse reaction (iv) has now been shown to occur. It seems fair to conclude that in base-catalysed thiol–disulphide interchange reactions the systems reach equilibrium with the more acidic thiol predominating. Since thiosulphuric acid possesses a low pK value [4] (1·24) for ionisation of the SH group, it is clear that many thiols and thiol-acids of lower acid strength are converted into disulphides by tetrathionate ion. Now, although *ionic* diethyldithiocarbamates (*e.g.*, the Na^+, or $Et_2NH_2^+$ salts) react readily and quantitatively with tetrathionate ion in the manner described (eqn. iv), it was found that *zinc* diethyldithiocarbamate underwent no detectable change in an aqueous methanolic solvent containing an equivalent of tetrathionate. Lack of reaction is not due to the insoluble nature of zinc diethyldithiocarbamate, since independent experiment shows that it is dissolved to the extent of at least 0·5% in the hot solvent used. These observations show that reaction (v) does not occur, and suggest that this may be due to the easier reverse reaction (vi), leading to the stable combination of tetrathionate ion and zinc diethyldithiocarbamate:

$$S_4O_6^{2-} + (Et_2N{\cdot}CS_2)_2Zn \underset{\text{(vi)}}{\overset{\text{(v)}}{\rightleftharpoons}} 2S_2O_3^{2-} + (Et_2N{\cdot}CS_2)_2 + Zn^{2+}$$

Experiments designed to test this prediction have now shown that sodium thiosulphate does not react with tetraethylthiuram disulphide (TET) alone but does so extremely readily, as shown in reaction (vi), if a soluble zinc salt capable of supplying Zn^{2+} ions is added to the system. This reaction proceeds as long as Zn^{2+} ions are present.

The reaction has been examined from the point of view of establishing the balance between reactants and products. The solvent used was methanol–water (5 : 1 v/v) in order to ensure solubility of starting materials, and temperatures were between 20° and 40°. From 0·02 mole of sodium thiosulphate, 0·01 mole of tetraethylthiuram disulphide, and 0·01 mole of zinc acetate there was obtained, after 30 min., 0·0094 mole of zinc diethyldithiocarbamate (isolated yield) and over 0·0090 mole of tetrathionate; also, 0·0196 mole of thiosulphate was consumed and a negligible amount of Zn^{2+} ions remained. That reaction only proceeds in the presence of Zn^{2+} ions was proved by allowing systems (where initially $2[S_2O_3^{2-}] > [Zn^{2+}] < [TET]$) to reach equilibrium and then measuring the correspondence between the initial quantity of zinc salt added and the thiosulphate ion which had reacted. This correspondence was found to be very good, *i.e.*, at least 1·94 g.-ions of thiosulphate react per g.-ion of zinc added.

The promotion of this otherwise unobservable interchange is by no means specific to Zn^{2+} ions. Similar reactions occur upon the addition of Cd^{2+} and Pb^{2+} ions to the thiosulphate–tetraethylthiuram disulphide combination, and there are preliminary indications that Co^{2+}, Ni^{2+}, Mn^{2+}, and Ag^+ ions behave similarly. Mg^{2+} and Ca^{2+} ions do not promote the interchange. The data do not permit definite conclusion to be drawn regarding the mechanism of these metal cation-assisted interchanges, but the following views are suggested.

A very obvious possibility is that the equilibrium (iii) $\rightleftharpoons$ (iv) is rapidly established but is normally well to the left of the equation so that reaction in the forward direction

[4] Kolthoff, *Rec. Trav. chim.*, 1924, **43**, 216.

(iii) is only observed experimentally if the dialkyldithiocarbamate ions are continuously removed by chelation with strongly bonding metal cations such as Zn^{2+}, Cd^{2+}, and Pb^{2+}.

A second possibility is that the metal cation is actually involved in the transition states of the substitutions at the sulphur atoms and is thereby exerting a genuine kinetic acceleration of the reaction in the forward direction.

Experimental

Materials.—Sodium dimethyldithiocarbamate was a pure sample kindly supplied by the Monsanto Chemical Co. Other compounds were either " AnalaR " materials or of the highest available purity. Potassium tetrathionate was made as follows: To iodine (12·7 g., 0·1 g.-atom) in ethanol (150 ml.) was added sodium thiosulphate (24·8 g., 0·1 mole) in water (30 ml.). Any iodine remaining after 10 min. was removed by cautiously adding more thiosulphate. Potassium iodide (20 g.) in water (10 ml.) was then added, and the solution cooled to 5—10°. The resultant crystalline potassium tetrathionate was recrystallised from ethanol–water (Found: S, 42·6. Calc. for $K_2S_4O_6$: S, 42·4%).

Reference Samples of Metal Dialkyldithiocarbamates.—To the sodium dialkyldithiocarbamate (0·02 mole) in water (20 ml.) were added methanol (80 ml.) and the requisite metal acetate (0·02/*n* mole, where *n* is the cationic charge) in water (20 ml.). The precipitated metal dialkyldithiocarbamate was collected, washed with methanol–water, dried, and recrystallised (usually from chloroform or toluene).

Reactions of Tetrathionate Ion with Dialkyldithiocarbamate Ions.—(i) *Dimethyldithiocarbamate ion.* To sodium dimethyldithiocarbamate ($2\frac{1}{2}H_2O$) (2·07 g., 0·011 mole) in water (50 ml.) was added potassium tetrathionate (1·51 g., 0·005 mole) in water (50 ml.). Tetramethylthiuram disulphide (1·18 g., 98·3%) was precipitated immediately and collected. It had m. p. (decomp.) *ca.* 150°, mixed m. p. 150—152° (Found: C, 30·1; H, 5·1. Calc. for $C_6H_{12}N_2S_4$: C, 30·0; H, 5·0%). The filtrate, after addition of excess of zinc acetate (to remove $Me_2N{\cdot}CS_2^-$ ions) and chloroform extraction, contained 0·0098 g.-ion of thiosulphate.

In a similar experiment a considerable excess of sodium dimethyldithiocarbamate (3·72 g., 0·02 mole) over the potassium tetrathionate (0·005 mole) was employed. Again, the yield of tetramethylthiuram disulphide was essentially quantitative. This reaction was therefore used to estimate gravimetrically tetrathionate produced in other reactions.

(ii) *Diethyldithiocarbamate ion.* To sodium diethyldithiocarbamate trihydrate (2·25 g., 0·01 mole) in water (50 ml.) was added potassium tetrathionate (1·51 g., 0·005 mole) in water (50 ml.), giving tetraethylthiuram disulphide (1·45 g., 98%), m. p. and mixed m. p. 69—70° (Found: C, 40·7; H, 6·9. Calc. for $C_{10}H_{20}N_2S_4$: C, 40·5; H, 6·8%). Similarly, diethylammonium diethyldithiocarbamate (from diethylamine and carbon disulphide in benzene–light petroleum) (2·22 g., 0·01 mole) gave 97% of tetraethylthiuram disulphide, m. p. 69—70°.

Stability of Zinc Diethyldithiocarbamate in Aqueous-methanolic Potassium Tetrathionate.—Zinc diethyldithiocarbamate (3·61 g., 0·01 mole) was refluxed for 3 hr. with potassium tetrathionate (3·02 g., 0·01 mole) in a mixture of methanol (100 ml.) and water (20 ml.). On cooling, the undissolved material was removed, and the filtrate evaporated under reduced pressure to remove most of the methanol. Water (50 ml.) was then added to the filtrate, and the resulting suspension extracted with chloroform (2 × 50 ml.). The undissolved material was added to the chloroform extracts which were then evaporated to dryness. Unchanged zinc diethyldithiocarbamate (3·54 g., 98%) was thus recovered, m. p. and mixed m. p. 177—178° (Found: C, 33·4; H, 5·5. Calc. for $C_{10}H_{20}N_2S_4Zn$: C, 33·2; H, 5·6. The aqueous filtrate after extraction was then analysed for tetrathionate ion as previously described (Found: 0·0075 g.-ion). The solubility of zinc diethyldithiocarbamate in the hot solvent employed was roughly checked as follows. The dithiocarbamate (2·0 g.) was used to saturate a mixture of methanol (100 ml.) and water (20 ml.) at reflux temperature. The hot mixture was rapidly filtered, and on cooling gave zinc diethyldithiocarbamate (0·61 g.), indicating a solubility of more than 0·5 g. per 100 ml. of refluxing solvent as used in the main experiment.

Reactions between Tetraethylthiuram Disulphide and Sodium Thiosulphate in the Presence of Zinc, Cadmium, and Lead Salts.—(i) *Zinc acetate.* To the disulphide (2·96 g., 0·01 mole) in warm methanol (100 ml.) was added sodium thiosulphate (4·96 g., 0·02 mole) in water (10 ml.). On addition of 10 ml. of M-zinc acetate precipitation of almost pure zinc diethyldithiocarbamate

(3·39 g., 0·0094 mole) occurred rapidly, m. p. and mixed m. p. (recrystallised from toluene) 177—178° (Found: C, 33·3; H, 5·6%). The filtrate, after evaporation under reduced pressure and extraction with chloroform, contained no ionic zinc (ethylenediaminetetra-acetic acid titration [5]) and only 2% of the original thiosulphate. It afforded tetramethylthiuram disulphide (2·12 g.), m. p. and mixed m. p. 152—154°, on treatment with excess of aqueous sodium dimethyldithiocarbamate; *i.e.*, the filtrate contained 0·0090 g.-ion of tetrathionate. The thiosulphate formed in this last process was also estimated by iodine titration as an additional check on the calculated tetrathionate value [after removal of excess of $Me_2N{\cdot}CS_2^-$ ions with zinc acetate (2·5 g.)]. (Zinc salts do not interfere with the titration of thiosulphate by iodine.) (Thiosulphate found: 0·019 g.-ion.)

(ii) *Zinc acetate in water.* The heterogeneous reaction was performed by refluxing tetraethylthiuram disulphide (0·01 mole), sodium thiosulphate (0·02 mole), and zinc acetate (0·01 mole) in water (100 ml.) for 3 hr. The mixture was cooled, and the insoluble material extracted with acetone (2 × 25 ml.), leaving zinc diethyldithiocarbamate (2·96 g., 0·0082 mole), m. p. 175—177°. A small quantity of material, mainly unchanged disulphide, was recovered from the acetone extract. The filtrate contained zinc ions (0·002 g.-ion), thiosulphate (0·0052 g.-ion), and tetrathionate (0·0042 g.-ion).

(iii) *Cadmium acetate.* To tetraethylthiuram disulphide (0·01 mole) in warm methanol (75 ml.) was added sodium thiosulphate (0·02 mole) in water (10 ml.). Then to the warm mixture was added cadmium acetate dihydrate (2·67 g., 0·01 mole) in warm water (15 ml.). Cadmium diethyldithiocarbamate was immediately precipitated (3·94 g., 0·00965 mole), m. p. 243°, mixed m. p. 244° (Found: C, 29·3; H, 5·1. Calc. for $C_{10}H_{20}N_2S_4Cd$: C, 29·4; H, 4·9%). On crystallisation from chloroform, it had m. p. and mixed m. p. 244—245° (Found: C, 29·5; H, 4·8%). The filtrate, examined as in (i), contained tetrathionate (0·00925 g.-ion).

(iv) *Lead acetate.* In an experiment performed precisely as for (iii), but with lead acetate trihydrate (3·79 g., 0·01 mole), there was isolated lead diethyldithiocarbamate as an amorphous light yellow powder, m. p. 205°, mixed m. p. 205—206° (Found: C, 24·2; H, 4·1. Calc. for $C_{10}H_{20}N_2S_4Pb$: C, 23·8; H, 4·0%). On crystallisation from chloroform it had m. p. and mixed m. p. 206—207° (Found: C, 23·9; H, 3·9%). The filtrate contained tetrathionate (0·00914 g.-ion, based on tetramethylthiuram disulphide obtained on treatment with sodium dimethyldithiocarbamate). The final thiosulphate ion check indicated tetrathionate ≡ 0·0090 g.-ion.

Additional Quantitative Experiments on the Reaction of Sodium Thiosulphate with Tetraethylthiuram Disulphide in the Presence of Zinc Salts.—The correspondence between Zn^{2+} ions added and $S_2O_3^{2-}$ ions which finally reacted was examined as follows. To 0·02M-methanolic disulphide (50 ml.) and 0·2M-aqueous sodium thiosulphate (10 ml.) were added various volumes

Relation between Zn^{2+} [*from* $Zn(OAc)_2$ *or* $ZnSO_4$] *added and* $S_2O_3^{2-}$ *ions used for systems TET* (*initially* 0·001 *mole*) + $Na_2S_2O_3$ (*initially* 0·002 *mole*) *in approx.* 60 *ml. of methanol–water* (5 : 1 *v/v*).

Zn^{2+} added (g.-ion × 10^{-4})	0·0	2·5	5·0	7·5	10·0 *	20·0
Thiosulphate used (g.-ion × 10^{-4})	0·0	4·6	9·7	14·8	19·4	19·6

* Equivalent to TET and $S_2O_3^{2-}$ taken.

(0—2·00 ml.) of M-zinc acetate or sulphate. After being left overnight, the reaction mixtures were filtered, and the filtrates extracted with chloroform (3 × 50 ml.) after addition of water (150 ml.). The final aqueous phase was titrated with standard iodine. The table expresses the correlation between Zn^{2+} ions added and $S_2O_3^{2-}$ used in the reaction. Almost identical results were obtained when cadmium and lead salts were used instead of zinc salts.

British Rubber Producers' Research Association,
48—56 Tewin Road, Welwyn Garden City, Herts. [*Received, December 5th*, 1959.]

[5] Schwarzenbach, "Complexometric Titrations" (trs. Irving), Methuen, London, 1957, p. 83.

552. *Magnetic Perturbation of Singlet–Triplet Transitions. Part III.*[1] *Benzene Derivatives and Heterocyclic Compounds.*

By D. F. Evans.

The singlet–triplet absorption bands of various monosubstituted benzene derivatives and monoaza-aromatic hydrocarbons have been measured, use being made of the perturbing effect of oxygen under pressure. The shifts of the benzene triplet level caused by different substituents are compared with those of the lowest singlet level. The spectra of the monoaza-aromatic hydrocarbons are very similar to those of the unsubstituted parent hydrocarbons, although characteristic small blue shifts are observed.

The very weak bands of pyrazine recently studied by Goodman and Kasha are considerably intensified by dissolved oxygen under pressure, confirming their assignment as singlet–triplet absorption bands.

Previous studies of the perturbing effect of oxygen under pressure have been extended to two main classes of organic compound, namely monosubstituted benzene derivatives and the monoaza-analogues of certain aromatic hydrocarbons.

Experimental

Measurements were made on a Unicam SP. 500 spectrophotometer as already described.[1,2] The compounds were purified by chromatography or fractional distillation. 1- and 2-Azaanthracenes were prepared as directed by Etienne.[3] Phenylcyclopropane was obtained by gentle refluxing of 5-phenyl-3-pyrazoline for *ca.* 1 hr., followed by slow distillation through a short column packed with glass helices. The distillate was shaken with ice-cold aqueous 1% potassium permanganate to remove methylstyrenes,[4] excess of sodium hydrogen sulphite solution was added, and the phenylcyclopropane washed, dried, and fractionally distilled (yield, *ca.* 50%; b. p. 173°). This modification of the usual method [5] is simpler and gives a better yield. The ultraviolet absorption spectrum in solution was in good agreement with that recorded by Robertson, Music, and Matsen.[6]

Results and Discussion

Benzene Derivatives.—The triplet levels obtained are given in Table 1, together with other results, and some of the spectra are illustrated in Fig. 1. The data are unfortunately not as extensive as could be desired, since in several cases (especially with compounds containing a group such as –OH which donates electrons to the benzene ring), the triplet bands are completely obscured by strong charge-transfer absorption.[1,7] Conversely, with compounds containing groups such as $-CF_3$ or –CN which withdraw electrons from the benzene ring and reduce its donor properties, the background charge-transfer absorption is less than that in benzene itself, although the triplet bands lie at longer wavelengths.

The triplet level of benzonitrile (26,880 cm.$^{-1}$) is in good agreement with that obtained from the phosphorescence spectrum (27,000 cm.$^{-1}$).[8] It is therefore clear that the extremely weak absorption bands at about 32,000 cm.$^{-1}$ observed by Hirt and King [9] for liquid benzonitrile and tentatively assigned as singlet–triplet bands, cannot in fact be due to transitions to the lowest triplet level of the benzonitrile molecule. Although it is possible that a higher triplet level is involved, it seems most likely that they are due to an impurity present in very small amount.

[1] Part II, Evans, *J.*, 1957, 3885.
[2] Evans, *J.*, 1957, 1351.
[3] Etienne, *Ann. Chim. France*, 1946, **1**, 1.
[4] Case, *J. Amer. Chem. Soc.*, 1934, **56**, 715.
[5] Hammond and Todd, *J. Amer. Chem. Soc.*, 1954, **76**, 4081.
[6] Robertson, Music, and Matsen, *J. Amer. Chem. Soc.*, 1950, **72**, 5260.
[7] Evans, *J.*, 1953, 345.
[8] Lewis and Kasha, *J. Amer. Chem. Soc.*, 1944, **66**, 2100.
[9] Hirt and King, *J. Chem. Phys.*, 1952, **20**, 1821.

XUM

The triplet level of nitrobenzene, as determined from its phosphorescence, has been reported to lie at 21,110 cm.$^{-1}$.[8] However, no absorption in this region was observed in the presence of oxygen under pressure. The perturbing effect of the oxygen may be inhibited by the strongly electron-attracting nitro-group, but it seems more likely that the observed phosphorescence is due to a triplet level in which the electron unpairing is essentially located in the nitro-group (n–π^* transition), or possibly to impurities.

TABLE 1. *Triplet levels (cm.$^{-1}$) of benzene derivatives by oxygen perturbation. (Chloroform solutions unless otherwise stated.)*

(Benzene	liquid	29,440 [a]	Phenylcyclopropane	~28,300	
	vapour	29,510 [b])	Benzonitrile	26,880	(phosphorescence 27,000) [c]
Fluorobenzene		29,500 [a]			
	vapour	29,530 [b]	Benzoyl chloride	26,280	
Benzotrifluoride	solution	29,150 *	Acetophenone	25,950	(phosphorescence 26,000 [d], 25,850 [f])
	vapour	29,150 *			
Toluene	solution	29,000 * (phosphorescence 28,889 [e], 28,900 [d])	Phenylacetylene	25,190	
			Styrene	21,600 [a]	
Methyl phenyl sulphone		28,700			
Chlorobenzene	vapour	28,570			

* 2,2,4-Trimethylpentane solution.

[a] Evans, *J.*, 1957, 1351. [b] Evans, *J.*, 1957, 3885. [c] Kanda and Sponer, *J. Chem. Phys.*, 1958, **28**, 798. [d] Dikun and Sveshnikov, *Zhur. eksp. teor. Fiz.*, 1949, **19**, 1000. [e] Lewis and Kasha, *J. Amer. Chem. Soc.*, 1944, **66**, 2100. [f] Terenin and Ermolaev, *Trans. Faraday Soc.*, 1956, **52**, 1042.

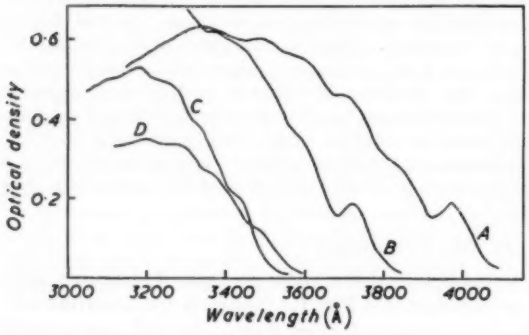


FIG. 1. *Light absorption of oxygen at* ca. 130 *atm. dissolved in solutions of benzene derivatives.* (5·2 *cm. cell.*)

A, 0·5M-Phenylacetylene in chloroform.
B, 1M-Benzonitrile in chloroform.
C, 0·4M-Benzotrifluoride in 2,2,4-trimethylpentane.
D, 0·5M-Methyl phenyl sulphone in chloroform.

TABLE 2. *Shifts (cm.$^{-1}$) of the lowest singlet and triplet levels of benzene to lower frequencies caused by various substituents.*

Substituent	Singlet *	Triplet	Substituent	Singlet *	Triplet	Substituent	Singlet *	Triplet
–F	270	50	–Cl	1037	940	$-NH_2$	4060	2670
$-CF_3$	270	350	–OH	1740	970	–CHO	1895	4270
$-CH_3$	616	580	cyclo-C_3H_5 ...	1228	~1240	–C≡CH	1719	4250
$-SO_2CH_3$ ...	850	740	–CN	1573	2560	$-CH=CH_2$ ...	3327	7840

* Except for $-SO_2CH_3$, vapour data from the literature were used.

In Table 2, the shifts (to higher frequencies) of the lowest benzene triplet level caused by different substituent groups are given (based partly on the present data and partly on phosphorescence spectra), together with the shifts of the lowest singlet level. This comparison is of interest since the effect of substituents on the lowest singlet level of benzene has been extensively studied [10] by using simple molecular-orbital theory. Recently Goodman and Shull [11] have applied an improved molecular-orbital theory with considerable success to both the singlet and triplet levels of certain monosubstituted benzene derivatives. Table 2 shows that if the substituent group does not contain a multiple bond conjugated

[10] Matsen, *J. Amer. Chem. Soc.*, 1950, **72**, 5243.
[11] Goodman and Shull, *J. Chem. Phys.*, 1957, **27**, 1388.

with the benzene ring, the shift of the triplet level is rather less than that of the singlet level, in agreement with Goodman and Shull's calculations. If, however, a multiple bond is present, the reverse is normally true. The $-SO_2{\cdot}CH_3$ group represents a special case. Although the S–O bonds probably possess considerable double-bond character, there is evidence that they do not conjugate appreciably with the benzene ring.[12]

FIG. 2.

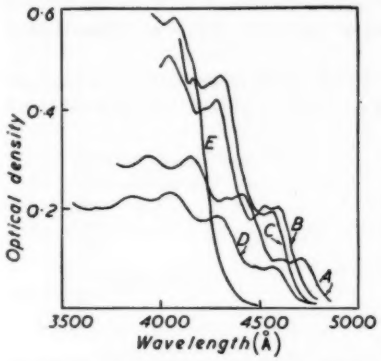


FIG. 3.

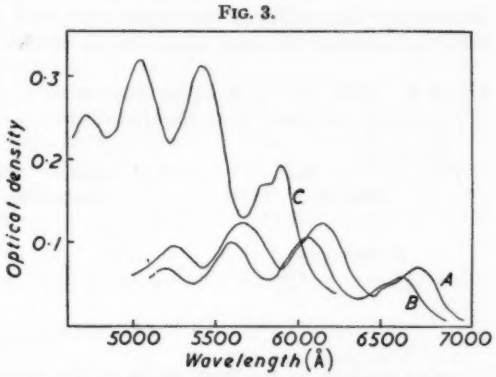


FIG. 2. *Light absorption of oxygen at* ca. 130 *atm. dissolved in* 0·5M*-chloroform solutions of heterocyclic compounds.* (5·2 *cm. cell.*)

A, Isoquinoline; max. at 21,210, 21,740, 22,650, 23,000, 24,040, 25,380 cm.$^{-1}$.
B, 7,8-Benzoquinoline; max. at 21,740, 22,000, 23,200, 24,540 cm.$^{-1}$.
C, 5,6-Benzoquinoline; max. at 21,880, 22,230, 23,340, *ca.* 23,700, 24,720 cm.$^{-1}$.
D, Quinoline; max. at 21,850, 22,350, 23,300, 23,750, 24,660, 25,900 cm.$^{-1}$.
E, Thionaphthen; max. at 23,970 cm.$^{-1}$.

FIG. 3. *Light absorption of oxygen at* ca. 130 *atm. dissolved in chloroform solutions of heterocyclic compounds.*

A, 0·92M-2-Aza-anthracene; max. at 14,870, 16,260, 17,650, 19,100 cm.$^{-1}$.
B, 0·37M-1-Aza-anthracene; max. at 15,070, 16,480, 17,860, 19,250 cm.$^{-1}$.
C, 0·5M-1-Azapyrene; max. at 16,930, 17,300, 18,450, 19,830, 21,170 cm.$^{-1}$.

Heterocyclic Compounds.—Results for monoaza-aromatic hydrocarbons are given in Figs. 2 and 3 and Table 3. The singlet–triplet absorption spectrum of a particular heterocyclic compound closely resembles that of the parent hydrocarbon as regards both the position of the 0,0 band and also the vibrational structure. By an appropriate shift of

TABLE 3. *Triplet levels* (*cm.*$^{-1}$) *of heterocyclic compounds in chloroform solution.* (*Accuracy about* $\pm$50 *cm.*$^{-1}$.)

Pyridine	29,650 $\pm$ 100 cm.$^{-1}$ [a]	Phenanthridine ...	~22,200
Quinoline	21,850 (P 21,700 [b])	Acridine	15,840 [c]
	21,840 (T)	2-Aza-anthracene	14,870
4-Methylquinoline ...	21,780	1-Aza-anthracene	15,070
Isoquinoline	21,210	1-Azapyrene [a] ...	16,930
5,6-Benzoquinoline ...	21,880	Thionaphthen ...	23,970 (P 24,010 [d],
7,8-Benzoquinoline ...	21,740		SP 23,917 $\pm$ 60 [e])

[a] Richter numbering.
[a] Evans, *J.*, 1957, 3885. [b] Lewis and Kasha, *J. Amer. Chem. Soc.*, 1944, **66**, 2100. [c] Evans, *J.*, 1957, 1351. [d] Heckman, *J. Mol. Spectroscopy*, 1958, **2**, 27. [e] Padhye and Patel, *J. Sci. Ind. Res., India*, 1956, **15**, *B*, 206.
P, phosphorescence at. SP, solvent perturbation at. T, in 2,2,4-trimethylpentane.

the frequency scale in each case, the main bands in the spectrum of an aromatic hydrocarbon can be made to coincide almost exactly with those of its monoaza-derivative. (The average deviation for 32 bands from 8 aza-compounds is only $\pm$20 cm.$^{-1}$.) This very close similarity in vibrational structure is not surprising, since the (ground-state) ring vibrational

[12] Barnard, Fabian, and Koch, *J.*, 1949, 2442.

frequencies of an aromatic hydrocarbon are little altered by substitution of a nitrogen atom.[13]

A rather similar situation is found with the normal (singlet–singlet) absorption spectra,[14] although since the bands are usually more diffuse the comparison is less accurate in this case.

The substitution of –N= for –CH= in various positions of an aromatic hydrocarbon does cause slight blue shifts of the triplet level, and values for these shifts (based on oxygen perturbation data obtained under similar conditions) are given in Table 4. They follow

TABLE 4. *Shifts (cm.$^{-1}$) to higher frequencies of the triplet levels of aromatic hydrocarbons caused by substitution of* –N= *for* –CH=. *Accuracy about* ±70 *cm.*$^{-1}$ (±130 *cm.*$^{-1}$ *for pyridine*).

Posn. subst.	Shift	Posn. subst.	Shift	Posn. subst.	Shift
Benzene		Anthracene		Phenanthrene	
—	200	1	200	1	280
		2	0	4	140
Naphthalene		9	970	9	~600
1	670				
2	30			Pyrene	
				1 *	0

* Richter numbering.

the same pattern as the (red) shifts of the singlet levels of the aromatic hydrocarbons caused by substituents such as $-CH_3$.[15] Thus, the largest effect is caused by substitution

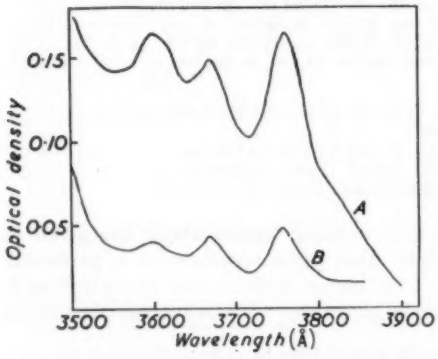


FIG. 4. *Light absorption of* 0·234M-*pyrazine in* 2,2,4-*trimethylpentane.* (5·2 *cm. cell.*)
A, Saturated with oxygen at *ca.* 130 atm.
B, In absence of oxygen. Max. at 26,600, 27,240 27,780 cm.$^{-1}$.

at the 9-position of anthracene, while in naphthalene and anthracene the effect is much greater for the 1- than the 2-derivative. There is a rough correlation between the triplet shifts and theoretical parameters for the aromatic hydrocarbons such as the free valency at the position substituted. However, a more precise interpretation would probably involve the *change* in the theoretical parameter in going from the ground state to the triplet level (cf. Pullman and Pullman [16]).

The intensities of the induced singlet–triplet bands (corrected for differences in concentration [2]) are appreciably smaller for the monoaza-compounds than for the parent hydrocarbons. The ratio of the intensities varies with the particular hydrocarbon studied, but is of the order of one half. In addition, except for pyridine, the short-wavelength charge-transfer absorption is less evident with the heterocyclic compounds. Both these

[13] Jones and Sandorfy, "Technique of Organic Chemistry," Vol. IX, Interscience, New York, 1956, p. 533.
[14] Badger, Pearce, and Pettit, *J.*, 1951, 3199.
[15] Peters, *J.*, 1957, 1993.
[16] Pullman and Pullman, "Progress in Organic Chemistry," Butterworths, London, 1958, Vol. 4, p. 31.

effects may be connected with the reduction of the π-donor characteristics of the aromatic hydrocarbon caused by the replacement of –CH= by –N=.[2]

Goodman and Kasha[17] observed three very weak bands around 3700 Å in the absorption spectrum of pyrazine, which were interpreted as arising from an n–π^* transition to the lowest triplet level of the pyrazine molecule. [The longest-wavelength band is at 26,553 cm.$^{-1}$, and the first phosphorescence band of pyrazine in EPA (ether–isopentane–alcohol) glass is at 25,991 cm.$^{-1}$.] The correctness of this assignment is shown by the results in Fig. 4. The spectrum in the absence of oxygen is in good agreement with that given by Goodman and Kasha, and subsequently by Hirt,[18] whilst the presence of oxygen at high pressure considerably increases the intensity of the absorption bands but does not affect their position. In this particular example, the *unperturbed* singlet–triplet absorption is of unusually high intensity (an explanation of this has been given [19]), and hence two characteristic features of oxygen perturbation are well illustrated. First, no appreciable shift of the singlet–triplet bands is caused by the dissolved oxygen; secondly the extent of the perturbation does not bear any relationship to the intensity of the unperturbed singlet–triplet absorption.

The author thanks Professor M. Kasha for sending him his results on pyrazine before publication.

INORGANIC CHEMISTRY RESEARCH LABORATORIES,
IMPERIAL COLLEGE, LONDON, S.W.7.

[*Received, March 25th*, 1959.]

[17] Goodman and Kasha, *J. Mol. Spectroscopy*, 1958, **2**, 58.
[18] Hirt, *Spectrochim. Acta*, 1958, **12**, 114.
[19] Sidman, *J. Mol. Spectroscopy*, 1958, **2**, 333.

---

553. *The Pentacyanohydride Complexes of Cobalt*(I) *and Rhodium*(I).

By W. P. GRIFFITH and G. WILKINSON.

High-resolution nuclear magnetic resonance studies have shown strong proton resonances characteristic of hydrogen atoms bound to the metal atom in reduced aqueous solutions of pentacyano-cobaltate and -rhodate ions; the species present are probably the ions $[HCo^{I}(CN)_5]^{3-}$ and $[HRh^{I}(CN)_5]^{3-}$. The cobalt species is found in low concentration in aqueous cobalt(II) cyanide solutions; in the light of this and other information the chemical properties of bivalent cobalt cyano-complex ions are discussed briefly.

The structures of $K_3[Co(CN)_3CO]$, $K_3[Co_2(CN)_8]$, and $K_3[Rh_2(CN)_8]$ are also discussed.

SEVERAL transition-metal complexes absorb molecular hydrogen and function as homogeneous hydrogenation catalysts;[1] it has often been suggested that in such systems species with a hydrogen atom bound to the metal atom are involved. Since it is now known [2] that abnormally large chemical shifts (14—22 p.p.m. on the high-field side relative to water) are characteristic for protons bound to transition-metal atoms, high-resolution nuclear magnetic resonance measurements provide the means for detecting such metal–hydrogen bonds in systems where it would otherwise be difficult to prove their presence.

Preliminary studies on the well-known cobaltous cyanide system showed that in the hydrogenated solutions a species giving a proton resonance signal in the characteristic region was present; however, it was found subsequently that hydrogenation is *not necessary*

[1] For references see: Halpern, *Quart. Rev.*, 1956, **10**, 463; Winfield, *Austral. J. Sci. Res.*, 1951, *A*, **4**, 385; Baston, Kelso King, and Winfield, "Advances in Catalysis," Academic Press, New York, 1957. Vol. 9, p. 312; Wender and Sternberg, *ibid.*, p. 594.
[2] Green, Pratt, and Wilkinson, *J.*, 1958, 3916, and references given therein.

and that the species is formed on dissolving cobaltous salts in cyanide solutions [3] or dissolving Adamson's salt, $K_6[Co_2(CN)_{10}]$, in water. In order further to elucidate this reaction and the nature of the hydrogen-containing metal species, we have studied reduced solutions of cobalt (and also rhodium) cyano-complexes; we discuss this aspect of the work first.

Reduction of Cobalt Cyano-complexes.—The green solutions of cobalt(II) cyano-species, from either a mixture of cobaltous salts and potassium cyanide or Adamson's salt, are reduced by potassium amalgam or sodium borohydride to yellow solutions. Previously, cobaltic species, *e.g.*, $[Co^{III}(CN)_6]^{3-}$, have been reduced both by potassium amalgam and electrolytically to give yellow solutions,[4] which were held to contain a univalent cobalt complex. Polarographic studies on cobaltous and cobaltic cyano-species have also shown evidence for reduction to a univalent cobalt species.[5,6,7]

The yellow solutions show a proton resonance at 695 ± 3 cycles/sec. (*vs.* the proton resonance of the water at 25° at 40 Mc./sec.), which confirms the diamagnetism of the cobalt species measured independently by the Gouy method. The fraction of the cobalt originally present which appears as the hydride cyano-ion was estimated by comparing the peak area of the proton resonance with a standard chloroform sample. This showed that essentially all of the cobalt was present as the hydride cyano-ion. The hydride species can be formed by reduction of cobalt cyanide solutions only when the CN^-/Co ratio is 5·0 or greater; if the ratio is less than five, metallic cobalt is deposited on treatment with amalgam or borohydride.

The likeliest possibilities for a monomeric, diamagnetic ion are $[HCo(CN)_4]^{2-}$ and $[HCo(CN)_5]^{3-}$. The former does not obey the inert-gas rule and would require a CN^-/Co ratio of 4; the latter obeys the inert-gas rule and its formation by direct reduction of pentacyanocobaltate(III) species as well as of cobaltous–cyanide solutions is understandable. Attempts to isolate the complex hydride ion as a solid salt have failed owing to its instability; *e.g.*, addition of alcohol results in evolution of hydrogen and precipitation of Adamson's salt:

$$2[HCo(CN)_5]^{3-} = [Co_2(CN)_{10}]^{6-} + H_2$$

whilst most precipitating cations are reduced; also ferroin gives a precipitate but this too decomposes rapidly.

Preliminary polarographic data [6] indicate that the number of cyanide groups in the reduced complex is the same as in $[Co(CN)_5H_2O]^{3-}$. These facts thus strongly suggest that the species is $[HCo(CN)_5]^{3-}$; this ion is isoelectronic with $HMn(CO)_5$ and Adamson's ion, $[Co_2(CN)_{10}]^{6-}$, is isostructural with $Mn_2(CO)_{10}$.[6]

TABLE 1. *Absorption spectra of cobalt cyano-complexes.*

Complex	Solvent	λ	ε	λ	ε	λ	ε	λ	ε	λ	ε
$[Co(CN)_5H_2O]K_3$ [a]	H_2O	960	3×10^3	640	10	430	50	350	500	278	6×10^3
$[Co_2(CN)_{10}]K_6$	$SOMe_2$	1030	3×10^3	330	20	286	5×10^3	272	6×10^3		
$[Co(CN)_5H]K_3$	H_2O	310	400	283	1300	268	2800				
H_2 + $[Co(CN)_5H_2O]K_3$ [a]	H_2O	960	260	510	80	320	4×10^3	285	3×10^3	268	3×10^3
$[Co(CN)_5H_2O]K_3$ [a] after 10 days' ageing	H_2O	960	40	575	10	350	10^3	285	3×10^3	268	3×10^3

[a] Parts of the spectra have also been described; see Kelso King and Winfield, *J. Amer. Chem. Soc.*, 1958, **80**, 2060; Winfield, personal communication.

In Table 1 is given the absorption spectrum of the yellow solution, and we consider that this represents the spectrum of the pure $[HCo(CN)_5]^{3-}$ ion. Dilute solutions (<0·1M) of the ion in presence of excess of borohydride are stable for at least a week as shown by absorption and nuclear magnetic resonance measurements. In concentrated solutions

[3] Griffith, Pratt, and Wilkinson, *Nature*, 1958, **182**, 466.
[4] Grübe, *Z. Elektrochem.*, 1926, **32**, 561; Treadwell and Huber, *Helv. Chim. Acta*, 1943, **26**, 10.
[5] Hume and Kolthoff, *J. Amer. Chem. Soc.*, 1949, **71**, 867.
[6] Vlček, personal communication.
[7] Maki, Fujita, and Tsuchida, *Nature*, 1959, **183**, 458.

(>~1M), however, hydrogen is slowly evolved and pentacyanoaquocobaltate(III) is produced.

TABLE 2. *Infrared spectra of some cyano-complexes (in Nujol mulls).*

[Absorptions in the C≡N and C=O stretching regions only are reported.]

Complex ...	$K_3[Co_2^{II}(CN)_{10}]$	$K_3[Co(CN)_5H_2O]$	$K_3[Co(CN)_6]$	$K_2[Co(CN)_5H_2O]$
Main bands	2133, 2090, 2079 [a]	2095 [b]	2143 [a]	2140 [b]
Complex ...	$K_3[Co(CN)_5OH],H_2O$ [a]	$Co_3[Co_2(CN)_{10}],5H_2O$	$K_6[Co_2(CN)_8]$	
Main bands	2135 (2114 vw, sh)	2133, 2085, 2063	2120, 2062	
Complex ...	$K_3[Rh(CN)_6]$	$K_3[Ir(CN)_6]$	$K_6[Rh_2(CN)_8]$	$[Fe(o\text{-phen})_3]_2[Co(CN)_5CO]$
Main bands	2163	2185	2130, 2070	2125, 2075, 1995, 1922

[a] Griffith and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 295. [b] In aqueous film between calcium fluoride plates.

The observation of the proton resonance line indicates that the proton bound to the cobalt atom has a chemical half-life in the solutions of at least 10^{-4} sec. (cf. the case of rhodium below).

Reduction of Rhodium Cyano-complexes.—Manchot [9] reported that hexacyanorhodate(III) solutions were reduced by hypophosphite to a univalent rhodium complex. We have found that if cyanide is added to the yellow (boiled) aqueous solutions (~1M) of rhodium trichloride the initial precipitate redissolves and that the solution can be reduced by sodium borohydride. The concentration of the hydride species produced in this case was high enough to enable the proton resonance spectrum to be observed in a 5 mm. o.d. spinning sample tube under conditions of resolution higher than in the cobalt case where dilute solutions in larger-diameter non-spinning tubes had to be employed. The rhodium solution shows a line at 625·5 ± 1 cycles/sec. on the high-field side relative to water at 40 Mc./sec. The assignment of the line as due to a proton bound directly to the metal atom is strengthened by the fact that the line is a symmetrical doublet with a separation of 13·1 ± 1 cycles/sec.; the width of each component is ⩽2 cycles/sec. This doublet splitting could be expected to arise in a covalent rhodium–hydrogen bond from the electron-coupled spin interaction between the proton and the rhodium nucleus (^{103}Rh, abundance 100%) which has spin ½. The observation of the doublet shows that the proton bound to the metal has a chemical lifetime of at least $1/(2\pi \times 13) \sim 0{\cdot}01$ sec. in this solution. In fact, the solutions sealed from air showed no change in the intensity of the proton resonance line, although there was little borohydride ion present during more than seven months.

Attempts to isolate salts of the complex ion failed, but by analogy with cobalt it is probably $[HRh(CN)_5]^{3-}$.

Polarographic reduction of rhodium trichloride in cyanide solutions is reported [10] to show an irreversible one-electron reduction at −1·47 v (*vs.* S.C.E.), but the value of $n = 1$ has recently been disputed.[11]

A later investigation showed no reduction at the dropping electrode.[12] Using a yellow solution of rhodium trichloride made 1M with respect to potassium cyanide, we find a well-defined irreversible reduction wave at $E_{\frac{1}{4}} = -1{\cdot}54$ v (*vs.* S.C.E.). The diffusion coefficient (D) being assumed to be the same as that for $[Co(CN)_5H_2O]^{3-}$,[5,10] application of the Ilkovič equation leads to a value of $n = 2{\cdot}0$, showing that as in the cobalt case the reduced species contains univalent rhodium.

Formation of $[HCo(CN)_5]^{3-}$ *in Aqueous Cobalt*(II)*–Cyanide Solutions.*—It was noted above that the resonance peak for $[HCo(CN)_5]^{3-}$ was first detected in solutions of cobaltous salts in presence of cyanide ions; the peak is at the same position as in the pure hydride and can be detected even in the freshly mixed solutions which are green and paramagnetic

[8] Griffith and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 295.
[9] Manchot and Schmid, *Ber.*, 1931, **64**, 2672.
[10] Willis, *J. Amer. Chem. Soc.*, 1944, **66**, 1067.
[11] Cozzi and Pantani, *J. Inorg. Nuclear Chem.*, 1958, **8**, 385.
[12] Rius and Molera, *Anales Fis. Quím.*, 1948, **44**, 53.

XUM

or in similar fresh solutions of Adamson's salt, $K_6[Co_2(CN)_{10}]$, after separation of the paramagnetic precipitate (see below). By comparison with a standard chloroform solution, the proportion of total cobalt in the form of the hydride ion appears to be about 3%. The intensity of the proton signal is unaffected by (*a*) increasing the cyanide concentration from $CN^-/Co = 5$ to 8, (*b*) saturating the freshly prepared green solutions with hydrogen, and (*c*) the ageing process of cobaltous–cyanide solution. Further, if the solutions are prepared in deuterium oxide from anhydrous salts, no proton resonance appears in the high-field region even when hydrogen has been passed through the solution for 1 hr. Since the resonance is found when solutions in water are prepared under nitrogen, these observations can only be interpreted to mean that the $[HCo(CN)_5]^{3-}$ ion must be formed by interaction of cobalt(II) and cyanide ions with water:

$$Co_{aq}^{2+} + 5CN^- + H_2O = [HCo^{I}(CN)_5]^{3-} + OH$$

We cannot explain why only 3% of the cobalt is transformed to the hydride; since the hydride appears to be formed instantaneously, is always present, and is unaffected by the subsequent changes in the cobalt–cyanide solutions (*e.g.*, ageing or hydrogen uptake), it is possible that the above reaction competes (unfavourably) with the presumably rapid aquation reaction of pentacyanocobaltate(II) ion to give $[Co(CN)_5H_2O]^{3-}$, as for example when the dimeric ion of Adamson's salt is cleaved in water.

The hydroxyl radical formed according to the above equation would undoubtedly oxidise the cobaltous bulk species, perhaps *via* a peroxy-complex.* Several workers have indeed reported the presence of peroxides during oxidation of cobalt(II) cyano-complex solutions.[13] A weak peak at 350 mμ in the absorption spectrum of a fresh solution of $[Co^{II}(CN)_5H_2O]^{3-}$ may well be attributed to a few units % of cobalt(III) species produced by hydroxyl radical reactions.

Nature of freshly prepared Cobaltous Cyanide Complex Solutions.—Apart from the small amounts of $[HCo(CN)_5]^{3-}$ and the corresponding cobaltic species, the components present in solutions of cobaltous ion in cyanide media freshly prepared in an inert atmosphere are probably as follows. (*a*) There is probably a small amount of a tetracyano-complex, most likely $[Co(CN)_4(H_2O)_2]^{2-}$. The existence of a tetracyano-cobalt complex in such solutions has been suggested by amperometric studies;[14] the corresponding tervalent cobalt complex $[Co(CN)_4(H_2O)_2]^-$ is known in solution.[15] Since clear solutions result when the ratio CN^-/Co is as low as 4·6 (precipitation begins at lower ratios), it seems necessary to assume that ions with a ratio CN^-/Co less than 5 are present. (*b*) The bulk of the solution species is undoubtedly a pentacyanocobaltate(II), either $[Co(CN)_5]^{3-}$ or $[Co(CN)_5H_2O]^{3-}$.[16] Although there has been considerable discussion concerning the nature of this ion, the latter formulation is favoured. Thus we find that the infrared spectrum of thin films of a fresh solution show only a single, very strong band in the C–N stretching region (at 2095 $cm.^{-1}$) similar to that in other pentacyanocobaltate species, $[Co(CN)_5X]^{3-}$.[8] † Polarography in non-cyanide media shows a direct reduction from $[Co(CN)_5H_2O]^{2-}$ to the cobalt(II) complex [5,6] and from $[Co(CN)_5X]^{3-}$ complexes to hexaco-ordinate cobalt(II) species.[7] The spin-only magnetic moment of 1·73 B.M. for the aqueous solutions [16,17] may also better support the

* Potassium cyanide reacts with the ion $[(NH_3)_5Co{\cdot}O_2{\cdot}Co(NH_3)_5]^{5+}$ in aqueous solution to give $[Co(CN)_5OH]^{3-}$, so that peroxycyano-complexes of cobalt, if they exist at all, must be unstable; we have been unable to find a report of such species in the literature.

† A pentacyano-hexaco-ordinate complex would be expected to show three C≡N stretches in accordance with its C_{4v} configuration; in fact, for all pentacyano-complexes examined only one intense peak is observed, with a small shoulder on this peak, and a very weak peak near 2200 $cm.^{-1}$. It is possible that higher resolution would have shown three distinct peaks.

[13] Peters, *Z. phys. Chem.*, 1898, **26**, 217; Manchot and Herzog, *Z. anorg. Chem.*, 1901, **27**, 404; Adamson, *Rec. Trav. chim.*, 1956, **75**, 809.

[14] Crémoux and Mondain-Merval, *Bull. Soc. chim. France*, 1949, 700.

[15] Smith, Kleinberg, and Griswold, *J. Amer. Chem. Soc.*, 1953, **75**, 149.

[16] Adamson, *J. Amer. Chem. Soc.*, 1951, **73**, 5710.

[17] Mills, Weller, and Wheeler, *J. Phys. Chem.*, 1959, **63**, 403.

aquated ion, since the odd electron is likely to occupy an *S*-state with no orbital contribution as in other inner orbital cobalt(II) ions, *e.g.*, $[Co(NO_2)_6]^{4-}$.[18] Finally, the absorption spectrum of $K_6[Co_2(CN)_{10}]$ is radically different in dimethyl sulphoxide from that in water (Table 1), as might be expected if a solvent molecule of such a different nature entered the co-ordination sphere.

Since the exchange of radio-CN^- with Adamson's salt [16] is unusually rapid, it seems likely that the water molecule in the aquated mononuclear ion is very weakly bound.

Precipitated Species, Ageing, and Hydrogen Absorption by Cobalt–Cyanide Solutions.—When the ratio CN^-/Co in Co^{II}–cyanide solutions is below 4·6, a green solid is deposited,[19] and when pure $K_6[Co_2(CN)_{10}]$ is dissolved in water a green solid is also deposited rather quickly (20 min.). This solid has been considered to be $K_2Co[Co(CN)_6]$,[20] but analyses and infrared measurements (Table 2) show that it is $Co^{II}_3[Co^{II}_2(CN)_{10}]$. There have been several reports [21] of cobaltous salts of cyano-complexes of Co^{II} and Co^{III}; some of these, which are red, are almost certainly cobaltous salts of the ion $[Co(CN)_5OH]^{3-}$.

It seems fairly clear from the results discussed above that the $[Co(CN)_5H]^{3-}$ ion is not a predominating factor in the ageing or the hydrogen-uptake process [17,19] of cobaltous cyanide solutions, and if complexes with metal–hydrogen bonds are involved in these cases the bonds must have an existence shorter than the nuclear magnetic resonance time scale. When the cobaltous–cyanide solution in deuterium oxide was saturated with hydrogen as noted above, a transformation of even 1% of the cobalt to $[HCo(CN)_5]^{3-}$ would have been detected; the only observable change was a slight increase in the intensity of the signal from the water contaminant in the deuterium oxide; this was of the right order of magnitude for the amounts of cobalt and hydrogen involved. The similarity of the absorption spectra (Table 1) for aged and hydrogenated fresh solutions of $[Co(CN)_5H_2O]^{3-}$ suggests that the final complexes may be the same in both cases and that a cobalt(I) species is produced. This was suggested for the hydrogenated solution by Mills *et al.*[17] In the case of the aged complex in dilute solution * the production of a cobalt(I) species from cobalt(II) must also produce an equivalent amount of cobalt(III), so that the process may be of the overall form:

$$2[Co^{II}(CN)_5H_2O]^{3-} = [Co^{I}(CN)_5H_2O]^{4-} + [Co^{III}(CN)_5H_2O]^{2-}$$

It may be noted that on addition of alcohol to either the yellow aged or the hydrogenated solutions a precipitate is obtained which appears to be a mixture of $K_6[Co_2(CN)_{10}]$ (purple-red) and $K_2[Co(CN)_5H_2O]$ (yellow) and whose infrared spectrum shows bands which would agree with those expected for a mixture; the former is presumably obtained by oxidation of a cobalt(I) species. The presence of $K_6[Co_2(CN)_{10}]$ is confirmed by the fact that dissolution of the mixed solid gives a green solution showing the appropriate absorption bands for $[Co(CN)_5H_2O]^{3-}$.

Other Cobalt and Rhodium Cyano-complexes.—The infrared spectrum (Table 2) of the ferroin salts of the tricyanocarbonyl cobaltate(I) ion,[22] $[Co^{I}(CN)_3CO]^{2-}$, shows three C–N and one C–O stretching frequency in agreement with its expected planar (C_{2v}) configuration. The octacyanodicobaltate(0) ion,[23] $[Co_2(CN)_8]^{8-}$, which is necessarily dimeric because of its diamagnetism, shows two C–N stretching modes in accordance with a D_{4h} configuration similar to that preferred [24] for the ion $[Ni_2(CN)_6(CO)_2]^{4-}$. A rhodium

* In concentrated ($> \sim 0{\cdot}5$M) solution $[Co^{II}(CN)_5H_2O]^{3-}$ evolves hydrogen [18] and the final product appears to be $[Co^{III}(CN)_5H_2O]^{2-}$.

[18] Figgis and Nyholm, *J.*, 1959, 338.
[19] Kelso King and Winfield, *J. Amer. Chem. Soc.*, 1958, **80**, 2060.
[20] Descampes, *Ann. Chim. Phys.*, 1878, **15**, 431.
[21] Alvarez, *Ann. Chim. Anal.*, 1910, **15**, 130; Benedetti-Pichler, *Z. anal. Chem.*, 1927, **70**, 258; Gmelin, "Handbuch der Anorganischen Chemie," Kobalt, Teil A, **58**, 1932 (Berlin, Verlag Chemie G.M.B.H.), pp. 377—379.
[22] Hieber and Bartenstein, *Z. anorg. Chem.*, 1954, **276**, 1.
[23] Watt, Hall, Choppin, and Gentile, *J. Amer. Chem. Soc.*, 1954, **76**, 373; Hieber and Bartenstein, *Naturwiss.*, 1952, **39**, 300; *Z. anorg. Chem.*, 1954, **276**, 12.
[24] Griffith, Cotton, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1959, **10**, 23.

analogue prepared by reduction of $K_3[Rh(CN)_6]$ with potassium in liquid ammonia is unstable and gave variable analyses; its infrared spectrum, however, is similar to that of the cobalt compound and it is probably $K_6[Rh_2(CN)_8]$.

Experimental

The salt $K_6[Co_2(CN)_{10}]$ was prepared by Adamson's method.[16] Cobaltous cyanide solutions were made from " AnalaR " salts under oxygen-free nitrogen. Rhodium and iridium hexacyanide complexes were prepared by published methods.[25,26]

Polarograms were obtained by using a Tinsley Mark 19 recording instrument with a dropping-mercury electrode [$C = 0{\cdot}56$ mole/l.; $m^{\frac{2}{3}}t^{\frac{1}{6}} = 1{\cdot}93$].

Absorption spectra were measured on a Perkin-Elmer Model 4000 recording spectrophotometer with 1-cm. stoppered silica cells; infrared spectra were taken on a Perkin-Elmer Model 21 recording spectrophotometer with sodium chloride optics.

High-resolution nuclear magnetic resonance measurements were made with a Varian Associates spectrometer at 40 Mc./sec., 5-mm. o.d. spinning tubes being used, or 15-mm. non-spinning tubes when necessary. The approximate measurements of $[HCo(CN)_5]^{3-}$ and $[HRh(CN)_5]^{3-}$ concentrations were made by comparing the peak area with that produced by a standard solution of chloroform in carbon tetrachloride under the same conditions of measurement.

Cobalt(II) *Decacyanodicobaltate*(II).—The green precipitate obtained on dissolving Adamson's salt in water was removed by centrifugation, washed with air-free water, and dried by alcohol and ether washes (Found: Co, 45·3. $Co_3[Co_2(CN)_{10}].5H_2O$ requires Co, 45·7%). No potassium could be detected in the solid *salt*. Its infrared spectrum shows the same bands as Adamson's salt.[8]

We thank the Department of Scientific and Industrial Research for a maintenance grant (W. P. G.), Messrs. Johnson, Matthey, and Co. Ltd. for loan of rhodium and iridium salts, and the United States Rubber Company for certain research expenses. We are indebted to Dr. L. Pratt for assistance with nuclear magnetic resonance measurements on the instrument provided by the D.S.I.R.

Inorganic Chemistry Research Laboratories,
Imperial College of Science and Technology,
London, S.W.7.

[*Received, March 26th*, 1959.]

[25] Krauss and Umbach, *Z. anorg. Chem.*, 1929, **179**, 359.
[26] Martius, *Annalen*, 1861, **117**, 357.

---

554. *The Infrared Spectra of Alkali Salts of Complex Fluoro-acids.*

By R. D. Peacock and D. W. A. Sharp.

The infrared spectra of a large number of alkali-metal salts of complex fluoro-acids have been recorded. The frequencies of the observed peaks are discussed in terms of the position of the central atom of the anion in the Periodic Table. It is concluded that complex fluorides, even in perovskite structures, show some covalent bonding in the central atom–fluorine bond. The infrared spectra of some complexes of unknown stereochemical configuration are discussed briefly.

Although much has been written about the metal–ligand bonding in complexes there are, in fact, few data on the bond strengths, most of the values being derived from stability constants of complexes in solution.[1] Since the stability constant of a complex is a measure of the free-energy change, this method of evaluating bond strengths involves the assumption that the entropy changes are approximately constant, and it is interesting to compare these

[1] Irving and Williams, *J.*, 1953, 3192.

values of bond strengths with values derived from a different method. The force constant for the symmetrical stretch of a metal–ligand bond should give some indication of the bond strength [2] but unfortunately the possibility of obtaining such force constants for a wide range of complexes is not great since the measurement of Raman spectra, which would be necessary to obtain the values of the symmetrical bond-stretching frequencies, is very difficult for this type of compound. Metal–oxygen stretching frequencies for a limited number of hydrates are known,[3] and these indicate that the order of stability of the hydrates is $Mn^{2+} < Cu^{2+} > Zn^{2+}$, *i.e.*, in agreement with the normal Irving–Williams order for the stability of complexes. The metal–oxygen symmetrical stretching frequency in acetylacetone complexes and benzoylacetone complexes follows the order of stability constants of the complexes.[4] The symmetrical stretching frequencies of a large number of chlorides, bromides, and iodides are known [5,6] and their values change in the same order as the stability constants where these are known. The metal–carbon stretching frequencies in a small number of complex cyanides have been discussed in terms of back-bonding from the metal to the ligand.[7]

Table 1 contains the absorption frequencies of some complex fluoro-anions and related compounds. All values refer to present work except where a reference is given. Except for the cryolites, the peaks are quite sharp and the position of the peak is characteristic of the particular complex fluoro-anion. In particular, it was found that the fluorosilicate ion, SiF_6^{2-}, was readily detected by the presence of a very characteristic band at 480 cm.$^{-1}$.

Tetrahedral.—Table 1 contains values for the infrared spectrum of K_2BeF_4 which has a broad peak of low intensity which is split into two components at 773 and 819 cm.$^{-1}$. This peak should be derived from the ν_3 vibration of a tetrahedral molecule, the band being split either because of the interaction of the ions in the unit cell or because of the low site symmetry of the ion in the crystal lattice (cf. the similar splitting of the 1100 cm.$^{-1}$ band of BF_4^- in potassium tetrafluoroborate [8,9]). Woodward [6] states that it has so far proved impossible to measure the Raman spectrum of the fluoroberyllate ion, so a precise discussion of the Be–F bond strength is not possible; however, it seems from the values of ν_3 that the BeF_4^{2-} ion follows the trend set by the isoelectronic entities BF_4^- and CF_4.

Octahedral.—By far the majority of complex fluorides have octahedra of fluoride ions about the central metal atom, these octahedra sometimes sharing corners. An octahedral molecule or ion, MF_6^{n-}, should have two (ν_3 and ν_4) infrared-active vibrations, and for the lighter atoms, M, two frequencies are observed in the region studied in the present investigation. By analogy with the gaseous molecules, MF_6, the absorption at the higher frequency is due to the vibration ν_3 and that at the lower to the vibration ν_4. Since ν_4 was not observed for all ions the present discussion will be confined to ν_3.

Qualitatively, the frequency of ν_3 decreases down a group of the Periodic Table and also decreases towards the more electropositive side of the Table. These changes are not completely regular and the slight irregularities will be discussed later. The first of these changes probably reflects the increase in mass of M. The second reflects the increase in the effective ionic radius of M, which is a measure of the decrease in the covalent character in the M–F bonds. The frequency of ν_3 decreases with decrease in valency of M, this trend again reflecting the increasing ionic character of the M–F bond with the increase in effective size of the M^{6-n} ion. The sharing of corners of octahedra does not greatly affect the frequency of ν_3 (see K_3AlF_6 and $KAlF_4$) and there is a regular change in the value of ν_3

[2] Cottrell, " The Strengths of Chemical Bonds," 2nd edn., Butterworths, London, 1958.
[3] Mathieu, *J. Chim. phys.*, 1953, **50**, C79.
[4] Nakamoto, McCarthy, and Martell, *Nature*, 1959, **183**, 459.
[5] Mathieu, *J. Inorg. Nuclear Chem.*, 1958, **8**, 33.
[6] Woodward, *Trans. Faraday Soc.*, 1958, **54**, 1271.
[7] Caglioti, Sartori, and Scrocco, *J. Inorg. Nuclear Chem.*, 1958, **8**, 87.
[8] Coté and Thompson, *Proc. Roy. Soc.*, 1952, **210**, *A*, 217.
[9] N. N. Greenwood, personal communication.

TABLE 1. *Infrared absorption frequencies of complex fluoro-ions (cm.$^{-1}$).*

Co-ordination number 4

BeF_4^{2-}	BF_4^- [a]	CF_4 [b]
773, 819	1100 (786)	1283 (903)

Co-ordination number 6

(i) Bivalent (measured in perovskites)

Mg		Cr	Mn	Fe	Co	Ni	Cu	Zn
462		481	407	431	439	445	489	437
Ca								Cd
<400								<400

(ii) Tervalent (measured in cryolites)

Al								
570 *								
Sc	Ti	V	Cr	Mn	Fe	Co		Ga
479	452	511	535, 522	560, 617 w	465 †	480		464
Y	Zr	Nb	Mo	Tc	Ru	Rh		In
<400	—	—	—	—	514, 497	530, 512		446
					479	500		
La								<Tl
<400								400

(iii) Quadrivalent

							Si
							(656) [c]
							726 ‡, 480
Ti	V	Cr	Mn	Fe	Co	Ni	Ge
560	583	556	622	—	—	654	600
Zr	Nb	Mo	Tc	Ru	Rh	Pd	Sn
<400	—	—	—	581	589	602	552
Hf	Ta	W	Re	Os	Ir	Pt	Pb
—	—	—	541	548	568	583	502
Th							
400							

(iv) Quinquevalent

							P [d]
							(741) §
							845, 559
V							As
715							700 §, 400
Nb	Mo	Tc	Ru				Sb
580	623	—	640				660
Ta	W	Re	Os	Ir			
580	594	627	616	667			

(v) Sexivalent

							S [e]
							965 (775)
							Se [f]
							787 (710)
							Te [f]
							752 (697)
	Mo						
	741 (741)						
	W [f]	Re [g]	Os	Ir [h]			
	712 (772)	716 (753)	—	718 (696)			
	U	Np [i]	Pu [i]				
	640 (656)	624 (648)	615 (628)				

Miscellaneous

AlF_4^- *				MnF_6^-			
599				614			
	ZrF_7^{3-}	NbF_7^{2-}	MoF_7^-	Tc		IF_6^-	
	<400	524	645	—		624	
		TaF_7^{2-}	WF_7^-	ReF_7^-	AuF_4^-		
		518	620	598	477, 585		

Figures in parentheses refer to the symmetrical stretching frequency, ν_1, observed from Raman spectra. All spectra of potassium salts except $CsReF_7$.

* For the AlF_6^{3-} anion de Lattre [j] finds 599 cm.$^{-1}$ for Na_3AlF_6 and records that $KAlF_4$ is similar.

† For the FeF_6^{3-} anion de Lattre [j] finds 492—458 cm.$^{-1}$ (diffuse) for Na_3FeF_6 and $(NH_4)_3FeF_6$.

‡ For the SiF_6^{2-} anion de Lattre [j] finds 735 and 488 cm.$^{-1}$ for K_2SiF_6.

§ The absorption bands thus marked have also been recorded previously.[k]

[a] Edwards, Morrison, Ross, and Schultz, *J. Amer. Chem. Soc.*, 1955, **77**, 266. [b] Woltz and Nielsen, *J. Chem. Phys.*, 1952, **20**, 307. [c] Siebert, *Z. anorg. Chem.*, 1953, **274**, 34. [d] Woodward, *J. Inorg. and Nuclear Chem.*, 1956, **3**, 326. [e] Landolt–Börnstein, "Atom- und Molekularphysik," Springer Verlag, Berlin, 1951. [f] Burke, Smith, and Nielsen, *J. Chem. Phys.*, 1952, **20**, 447. [g] Gaunt, *Trans. Faraday Soc.*, 1954, **50**, 209. [h] Mattraw, Hawkins, Carpenter, and Sabol, *J. Chem. Phys.*, 1955, **23**, 985. [i] Malm, Weinstock, and Classen, *ibid.*, 1955, **23**, 2192. [j] de Lattre, *J. Chem. Phys.*, 1952, **20**, 1180. [k] Sharp and Sharpe, *J.*, 1956, 1855.

from the volatile MF_6 compounds to the perovskites, KMF_3, where the bonding is supposed to be purely ionic. There is no great difference between the frequencies found for transitional and B-group, non-transitional, complexes. These qualitative observations appear to support the formulation of all the MF_6^{n-} groups as complexes with a constant, or smoothly changing, order of covalent character. From the mere fact that the infrared spectra of perovskites are observable between 400 and 500 cm.$^{-1}$ it appears that there is some covalent bonding even in these compounds.

Quantitative consideration of these results is much more arbitrary. Ideally one would like to consider the symmetrical stretching force constant of the M–F bond but this can only be derived from Raman spectra. The Tables show that for molecules and ions where ν_3 and ν_1 are both known there is no direct relation between these two frequencies. This is borne out by calculations made on an octahedral group, MX_6, using various force fields.[10,11] The abrupt change in the value of $\nu_1 - \nu_3$ on passing from the series SF_6, SeF_6, TeF_6 to UF_6 has been discussed and tentatively recognised as being due to a change in the type of hybridisation in passing from the B to the A sub-group.[12] The fact that the frequency of ν_1 for MoF_6 is less than the value for WF_6 indicates an unexpected change in the force constant between these two compounds. However, one may hope that for a series of molecules or ions of similar mass, trends in ν_3 should follow trends in ν_1 and that this in turn can be related to changes in the force constant K_1. For example, in the isoelectronic series of ions SF_6, PF_6^-, SiF_6^{2-}, and AlF_6^{3-} (Table 2) it can be considered that the values of ν_1 and K_1 for AlF_6^{3-} would follow the trend set by the other ions, the force constant being smaller than that for the SiF_6^{3-} ion.

TABLE 2.

	ν_1 (cm.$^{-1}$)	10^5K_1 (dynes cm.$^{-1}$) [6]	ν_3 (cm.$^{-1}$)
AlF_6^{3-}	—	—	570
SiF_6^{2-}	656	4·82	726
PF_6^-	741	6·14	845
SF_6	775	6·72	965

(For other references see Table 1.)

Theories on bond strengths for transition-metal–ligand bonds use two approaches. The ionic radius [13] and thus the interatomic separation [14] can be considered in terms of the crystal-field stabilisation of the complex. For octahedral ions this would predict a maximum contraction, *i.e.*, maximum bond strength, for d^3 and d^8 configurations, with complications arising from the Jahn–Teller distortion of the d^4 and d^9 configurations. Results on $M^{2+} \ldots . F^-$ separations [14] follow crystal-field predictions but there are notable gaps at the d^4 and d^9 configurations since meaningful octahedral radii cannot be obtained for Cr^{2+} and Cu^{2+}. The alternative approach is to relate the bond strength to the tendency towards covalent-bond formation [1,15] between ligand and cation, this tendency being measured by the appropriate ionisation potential. Williams [15] points out that the crystal-field approach as applied to the stability of complexes leaves much to be desired, especially when considering the d^4 and d^9 configurations. Qualitatively, for MF_6^{4-} and MF_6^{3-} ions the observed values of ν_3 follow the $M^+ \longrightarrow M^{2+}$ and $M^{2+} \longrightarrow M^{3+}$ ionisation potentials respectively, the agreement being particularly good over the d^4 to d^{10} configurations. There appear to be irregularities for the d^0 and d^1 (ScF_6^{3-} and TiF_6^{3-}) configurations for the MF_6^{3-} ions and for the d^2 (CrF_6^{2-}) configuration for the MF_6^{2-} series but the appropriate

[10] Venkateswarlu and Sundaram, *Z. phys. Chem.* (*Frankfurt*), 1956, **9**, 174.
[11] Pistorius, *J. Chem. Phys.*, 1958, **29**, 1328.
[12] Heath and Linnett, *Trans. Faraday Soc.*, 1949, **45**, 264.
[13] Hush and Pryce, *ibid.*, 1957, **26**, 143.
[14] Hush, *Discuss. Faraday Soc.*, 1958, **28**, 145.
[15] Williams, *ibid.*, p. 123.

ionisation potentials are not accurately known. It seems, therefore, that the present measurements are in accordance with the idea of electron transfer from ligand to cation.

As stated, d^4 and d^9 configurations should show Jahn–Teller splitting resulting in distortion of the regular octahedral co-ordination.[14] Such distortion might cause splitting in the vibrational frequencies. No splitting is observed with the complexes $KCrF_3$ and $KCuF_3$ (preliminary experiments [16] showed a splitting but re-preparation removed the extra bands which must have been due to hydrolysis) and it must be assumed either that the extra bands are too weak or that the splitting is too small for observation. Crystallographically $KCrF_3$ [17] and $KCuF_3$ [18] are not isostructural with the perovskites. K_3MnF_6, which seems to show distortion in its crystal structure,[19] does have an extra infrared band at 617 cm.$^{-1}$.

Observations could not be made on all possible quadrivalent complexes. The d^4 complex, K_2FeF_6, does not exist and the d^5 complex Cs_2CoF_6, does not give good infrared spectra. K_2NiF_6 is the only element in the first transition series to give a spin-paired complex fluoride.[20] The position of the peak cannot be adequately compared with that expected for a spin-free complex as this would involve extrapolation over a gap of two elements but a simple comparison indicates that the change from a spin-free to a spin-paired configuration does not greatly affect the bond strength as estimated by the present method.

In addition to the weak extra peak observed for K_3MnF_6, the main peak in many other cryolites is split into several components of approximately equal intensity. It has been noted that cryolite structures are particularly prone to slight departures from ideality, these distortions being variously explained as being due to changes of composition [21] or to temperature effects causing rotation of the MF_6^{3-} octahedra.[22] The first of these effects might cause splitting of the fundamental vibrations because of the lowering of site symmetry of the complex ion; rotation effects should tend to increase the symmetry of the complex ion. The presence of more than one molecule in the unit cell might cause splitting of the infrared peaks.

The second- and third-period transition elements show fairly regular trends across the Periodic Table. The rather large drop in the observed infrared frequency on passing from K_2TiF_6 to K_2ZrF_6 is probably due to the change in co-ordination number of M from 6 to 8 in going from titanium to zirconium; [23] K_3ZrF_7, where zirconium is heptaco-ordinate, also has a low value. For pairs of elements where the lanthanide contraction is showing its maximum effect (*e.g.*, Nb, Ta), the observed infrared peaks are close together.

Miscellaneous.—Addition of a fluoride ion to an MF_6^{n-} anion lowers the observed infrared frequency. It cannot be said whether the observed vibration bears any relation to the infrared frequencies observed for octahedral ions. The observation of an infrared peak for $KMnF_5$ at 614 cm.$^{-1}$ as compared with 622 cm.$^{-1}$ for K_2MnF_6 suggests that the co-ordination is octahedral in the $KMnF_5$; a discrete MnF_5^- ion should give absorption at a frequency very much higher than that observed for the MnF_6^{2-} ion (cf. NbF_7^{2-} and NbF_6^-). The presence of only one peak in the spectrum of KIF_6 suggests a fairly symmetrical structure for the IF_6^- ion; the structure of this ion should be heptaco-ordinate with one position occupied by a lone pair of electrons. The ions of similar electronic structures, $TeCl_6^{2-}$, $TeBr_6^{2-}$, appear to be effectively spherical in the crystalline state even if they are not actually octahedral (for a discussion of the structure of these ions see reference 24).

[16] Sharp, *Discuss Faraday Soc.*, 1958, **28**., 186.
[17] Edwards and Peacock, unpublished observations.
[18] Martin, Nyholm, and Stephenson, *Chemistry and Industry*, 1956, 83.
[19] Peacock, *J.*, 1957, 4684.
[20] Klemm and Huss, *Z. anorg. Chem.*, 1949, **258**, 221.
[21] Brosset, *Arkiv Kemi, Min., Geol.*, 1946, **21**, *A*, 142.
[22] Bode and Voss, *Z. anorg. Chem.*, 1957, **290**, 1.
[23] Bode and Teufer, *Acta Cryst.*, 1956, **9**, 929.
[24] Emeléus and Sharpe, *J.*, 1949, 2206.

XUM

$KAuF_4$ shows two distinct infrared peaks. This salt appears isomorphous with $KBrF_4$,[25] having square planar co-ordination about the central gold atom. This structure, however, does allow further interaction between gold and fluorine atoms belonging to another AuF_4^- group to give distorted octahedral symmetry about the gold atom (cf. the structure of $KBrF_4$ [26]); such a structure would be expected to show extra infrared bands. It has recently been pointed out [27] that similar distorted octahedra can be considered to occur in the complexes $Cs_2AgCl_2AuCl_4$ and $Cs_2AuCl_2AuCl_4$.[28]

Experimental

The complex fluorides were prepared by the standard literature methods. Infrared spectra were measured in Nujol or hexachlorobutadiene mulls, and, where the salts were stable to traces of moisture, in potassium bromide pressed discs. Mulls were prepared in the dry-box. Spectra were recorded on a Perkin-Elmer Model 21 recording spectrophotometer with rock-salt or potassium bromide optics. Specimens of K_3NiF_6 and K_3CuF_6 would not give good infrared spectra. The infrared band of K_3CoF_6 is extremely broad and it is believed that the peaks of the present compounds are so broad as to preclude observation. Cs_2CoF_6 immediately attacked Nujol and satisfactory infrared spectra could not be obtained.

We thank Messrs. A. J. Edwards and G. B. Hargreaves for the preparation of some of the samples; also Johnson, Matthey and Co. Ltd. for the loan of precious metals and Imperial Chemical Industries Limited for the gift of bromine trifluoride and for the loan of a fluorine cell.

Chemistry Department,
University of Birmingham,
Edgbaston, Birmingham, 15 (R. D. P.).
Inorganic Chemistry Research Laboratories,
Imperial College of Science and Technology,
London, S.W.7 (D. W. A. S.).

[*Received, April 24th*, 1959.]

[25] Peacock, unpublished observations.
[26] Sly and Marsh, *Acta Cryst.*, 1957, **10**, 378.
[27] Harris, *J.*, 1959, 682.
[28] Elliot and Pauling, *J. Amer. Chem. Soc.*, 1938, **60**, 1846.

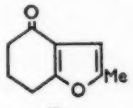
---

555. *Some Experiments with Furans.*

By D. A. H. Taylor.

γ-(5-Methyl-2-furyl)butyric acid has been synthesised from 2-methylfuran, and cyclised to give 4,5,6,7-tetrahydro-2-methyl-4-oxobenzofuran.

The thiophen analogue of α-tetralone has been described by Fieser and Kennelly,[1] but the related furan compound has not been prepared. This paper records the synthesis of the 2-methyl derivative (I) of this compound. In early attempts to acylate 2-methylfuran with succinic anhydride, either no reaction occurred or the furan resinified, perhaps partly owing to the insolubility of succinic anhydride.



(I)

The possibility of carrying out a Hoesch reaction on furan, mentioned by Reichstein,[2] does not seem to have been tested. Chloroacetonitrile was found to give a fair yield of 2-chloroacetyl-5-methylfuran, but this product did not react satisfactorily with diethyl malonate.

γ-2-Furylbutyric acid was made by Hofmann *et al.*[3] from 3-2′-furylpropanol by conversion into the chloride and nitrile, but the yield was not high. The alcohol was made by the catalytic reduction of 3-2′-furylacraldehyde. In our hands this reduction proved capricious. The more readily available β-2-furylacrylic acid has been reduced catalytically,

[1] Fieser and Kennelly, *J. Amer. Chem. Soc.*, 1935, **57**, 1611.
[2] Reichstein, *Helv. Chim. Acta*, 1930, **13**, 356.
[3] Hofmann, Bridgwater, and Axelrod, *J. Amer. Chem. Soc.*, 1949, **71**, 1253.

but this reduction also proved difficult to repeat. The best method of reducing arylacrylic acids is often by means of Raney alloy in sodium hydroxide solution, which has been reported to reduce β-2-furylacrylic acid to a mixture of tetrahydrofurylpropionic acid and propylbutyrolactone.[4] By the use of milder conditions, β-2-furylpropionic acid was obtained in good yield. Reduction of this with lithium aluminium hydride in ether gave the corresponding alcohol, whose benzenesulphonate on reaction with sodium cyanide followed by hydrolysis gave γ-2-furylbutyric acid in good yield.

Attention was then turned to the 2-methyl derivative. 5-Methylfurfuraldehyde has been prepared from 2-methylfuran in 76% yield by the dimethylformamide synthesis without the use of a solvent.[5] In ethylene dichloride, the yield was 95%. With one equivalent of malonic acid in pyridine, this gave 83% of β-(5-methyl-2-furyl)acrylic acid,[6] while with 1·2 equivalents, the yield was 87%. Reduction with Raney alloy in alkaline solution then gave β-(5-methyl-2-furyl)propionic acid, which was converted into the butyric acid by the method described above. Cyclisation of this with phosphorus pentachloride and stannic chloride in benzene gave the required 4,5,6,7-tetrahydro-2-methyl-4-oxobenzofuran (I).

This ketone with methylmagnesium bromide gave only a small yield of the expected product, the residue being polymeric. This is not the case with the thiophen analogue, which reacted normally. Reduction of β-2-furylacrylic acid by lithium aluminium hydride gave a product which was probably the corresponding allyl alcohol, thus providing another case, contrary to early reports, where the double bond in an acrylic acid is not reduced by this reagent.

Experimental

2-Chloroacetyl-5-methylfuran.—2-Methylfuran (36 g.) and chloroacetonitrile (33 g.) were dissolved in dry ether (200 ml.) and saturated with hydrogen chloride at 0°. After storage at 0° overnight the solvent was decanted, and the deep blue crystalline deposit decomposed with water. The oil which separated was extracted with methylene chloride, dried, recovered, and crystallised from ether, to give *2-chloroacetyl-5-methylfuran* (24 g., 34%) as prisms, m. p. 70° (Found: C, 53·0; H, 4·6. $C_7H_7O_2Cl$ requires C, 53·0; H, 4·45%); this substance was a strong skin-irritant.

5-Methylfurfuraldehyde.—Phosphorus oxychloride (250 ml.) was added to dimethylformamide (200 g.) with stirring and ice-cooling during 10 min. The mixture was diluted with ethylene dichloride, and 2-methylfuran (187 g.) in ethylene chloride (250 ml.) added with stirring in 1 hr. below 20°. After 2 hr. at room temperature the solution was brought to reflux, then cooled, and added to a solution of sodium acetate (1800 g. hydrated) in water (2·5 l.), refluxed for 15 min., and cooled. The organic layer was washed with sodium carbonate solution and with water, then evaporated, and the residue distilled. 5-Methylfurfuraldehyde (239 g., 96%) was collected at 64°/7 mm. as a pale yellow oil, n_D^{30} 1·5237.

β-(5-Methyl-2-furyl)acrylic Acid.—5-Methylfurfuraldehyde (239 g.), malonic acid (258 g.), and pyridine (125 ml.) were heated on the steam-bath for 3 hr. After cooling, the crystalline mass was diluted with aqueous hydrochloric acid, and the product (287 g., 87%) filtered off and dried in a desiccator. A specimen formed colourless needles, m. p. 152—153°, from aqueous methanol. Kuhn *et al.*[6] give m. p. 153—154°.

β-(5-Methyl-2-furyl)propionic Acid.—The above acid (146 g.) was dissolved in water (1 l.) containing sodium hydroxide (40 g.), and Raney alloy (100 g.) was added. The suspension was stirred in an ice-bath, and a solution of sodium hydroxide (80 g.) in water (300 ml.) was added, the temperature being kept below 20°. The solution was then stirred at 30° for 2 hr. After filtration, the solution was acidified with tartaric acid (250 g.) in water (500 ml.) and concentrated hydrochloric acid (150 ml.) and extracted with ethyl acetate (2 × 500 ml.). The extract was washed, dried, and evaporated. The residue crystallised from light petroleum (b. p. 40—60°) to give β-(5-methyl-2-furyl)propionic acid (114 g., 78%) as needles, m. p. 55—58°.

[4] Papa, Schwenk, and Ginsberg, *J. Org. Chem.*, 1951, **16**, 253; *Org. Synth.*, Coll. Vol. III, p. 742.
[5] Traynelis, Miskel, and Sowa, *J. Org. Chem.*, 1957, **22**, 1269.
[6] Kuhn, Köhler, and Köhler, *Z. physiol. Chem.*, 1937, **247**, 197.

Recrystallisation from n-pentane raised the m. p. to 57—57·5° (Robinson and Todd [7] give m. p. 54—55°, Wichterle gives m. p. 61—62°) (Found: C, 62·25; H, 6·65. Calc. for $C_8H_{10}O_3$: C, 62·3; H, 6·5%). The p-*bromophenacyl ester* formed laths, m. p. 103—104°, from methanol (Found; C, 55·9; H, 4·6. $C_{15}H_{15}O_3Br$ requires C, 55·75; H, 4·6%).

β-2-Furylpropionic acid, obtained similarly, had m. p. 58°.

3-(5-*Methyl*-2-*furyl*)*propan*-1-*ol*.—The above acid (130 g.) in ether (500 ml.) was added gradually to lithium aluminium hydride (40 g.) in ether (1 l.). The solution was decomposed with water, and a solution of sodium tartrate (500 g.) and concentrated hydrochloric acid (150 ml.) in water was added. The ether layer was separated, the aqueous layer extracted again with ether, and the combined ether layers washed and evaporated. Distillation of the residue gave 3-(5-methyl-2-furyl)propan-1-ol (112 g., 95%), b. p. 94°/3 mm., n_D^{30} 1·4775. The α-*naphthylurethane* formed needles, m. p. 94—95°, from light petroleum (b. p. 100—120°) (Found: C, 73·8; H, 6·3. $C_{19}H_{19}O_3N$ requires C, 73·8; H, 6·2%).

3-2′-Furylpropan-1-ol, prepared similarly, had b. p. 96°/8 mm., n_D^{30} 1·4719. Reduction of β-2-furylacrylic acid gave an oil, b. p. 110°/7 mm., n_D^{27} 1·5311.

γ-(5-*Methyl*-2-*furyl*)*butyric Acid*.—3-(5-Methyl-2-furyl)propan-1-ol (104 g.) and pyridine (200 ml.) were stirred, and benzenesulphonyl chloride (150 g.) was added in 2 hr. so that the temperature remained below 20°. After a further 2 hr. ice was added, and the whole poured into ice-water (1 l.) and ether, the ether extract was dried and evaporated, and the residue in methanol (250 ml.) refluxed with sodium cyanide (46 g.) in water (100 ml.) for 12 hr. After cooling, water and ether were added, and the extract was washed, dried, and evaporated. Distillation gave 4-(5-*methyl*-2-*furyl*)*butyronitrile* (69 g., 61%), b. p. 91°/2 mm., n_D^{20} 1·4710. The distillation residue was mostly the acid, and it was combined with the nitrile and the whole refluxed for 12 hr. with sodium hydroxide (42 g.) in water (120 ml.). After acidification, the product was extracted with ether, crystallisation from n-pentane then gave γ-(5-*methyl*-2-*furyl*)*butyric acid* (87 g., 70%) as rhombs, m. p. 57—58° (Found: C, 64·5; H, 7·2. $C_9H_{12}O_3$ requires C, 64·3; H, 7·2%). γ-2-Furylbutyric acid was obtained similarly; the nitrile had b. p. 110°/8 mm., n_D^{20} 1·4695.

4,5,6,7-*Tetrahydro*-2-*methyl*-4-*oxobenzofuran*.—γ-(5-Methyl-2-furyl)butyric acid (73 g.) in benzene (600 ml.) was treated with phosphorus pentachloride (91 g.) with stirring at 0°. After ½ hr. stannic chloride (53 ml.) in benzene (100 ml.) was added with stirring below 5°. An orange solid began to separate at once. The whole was stirred for ½ hr. and added to ice-water and toluene. The organic layer was washed with cold dilute hydrochloric acid, with potassium carbonate solution, and with water, dried, and evaporated. Distillation gave 4,5,6,7-*tetrahydro*-2-*methyl*-4-*oxobenzofuran* (51 g., 77%), b. p. 104°/2 mm., n_D^{24} 1·5235 (Found: C, 71·2; H, 6·8; O, 22·1. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7; O, 21·3%). The *dinitrophenylhydrazone* formed dark red prisms, m. p. 255—257°, from chloroform–ethanol (Found: C, 54·5; H, 4·2; O, 24·4; N, 17·1. $C_{15}H_{14}O_5N_4$ requires C, 54·5; H, 4·3; O, 24·2; N, 17·0%).

Grignard Reaction with 4,5,6,7-*Tetrahydro*-2-*methyl*-4-*oxobenzofuran*.—A Grignard solution was prepared from magnesium (14 g.) and methyl bromide in ether (500 ml.). To this was added the above ketone (71 g.) in ether (200 ml.). After the addition was complete, the complex was decomposed with aqueous ammonium chloride, and the ether layer dried and evaporated. Distillation of the residue gave a product, either 6,7-dihydro-2,4-dimethylbenzofuran or the exocyclic isomer (27 g., 39%), b. p. 72°/2·5 mm., $\lambda_{max.}$ 242 mμ (log ε 3·76 in cyclohexane) (Inflection only, with strong end-absorption). No OH group was detectable by the infrared spectrum. The residue was a water-clear gum that did not distil below 200°/2·5 mm.

Grignard Reaction with 4,5,6,7-*Tetrahydro*-4-*oxobenzothiophen*.—To a Grignard solution from magnesium (6 g.) and methyl bromide in ether (250 ml.) the above ketone (25 g.) was added in ether. The complex was decomposed with aqueous ammonium chloride, and the ether layer dried and evaporated. Distillation of the residue gave 6,7-dihydro-4-methylbenzothiophen (or the double-bond isomer) (21 g.), b. p. 130°/14 mm., $\lambda_{max.}$ 229 mμ (log ε 4·3 in cyclohexane) (no OH band in the infrared spectrum).

UNIVERSITY COLLEGE, IBADAN. [*Received, April 6th*, 1959.]

[7] Robinson and Todd, *J.*, 1939, 1743.
[8] Wichterle, *Coll. Czech. Chem. Comm.*, 1939, **11**, 171.

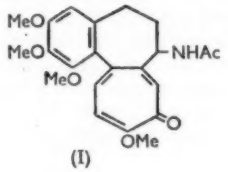
XUM

556. *Photochemical Transformations of Tropolones. Part I. Tetra-O-methylpurpurogallin.*

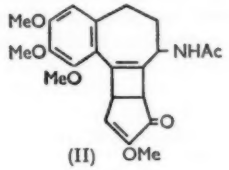
By E. J. Forbes and R. A. Ripley.

Dilute aqueous-alcoholic solutions of tetra-*O*-methylpurpurogallin (III) in sunlight give a number of products, including methyl 6,7,8-trimethoxy-1-naphthoate (VI). The course of the reaction is discussed.

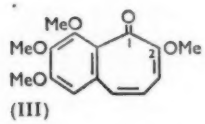
Apart from a recent communication on γ-tropolone methyl ether [1] the photosensitivity of simple tropolones appears to have passed unreported. Of the more complex tropolones, only colchicine (I) has been investigated. It is converted in aqueous solution by sunlight into three isomers,[2] two of which have been shown to have stereoisomeric structures [3] (II), for which confirmatory evidence has been adduced by Gardner *et al.*[4] These results demonstrate that at least the tropolone ring has been involved in the transformations. For closer study we have investigated the action of light on a number of simple tropolones and the readily available tetra-*O*-methylpurpurogallin (III). The last compound gave an unexpected result.



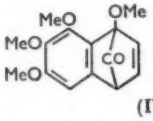
(I)



(II)



(III)



(IV)

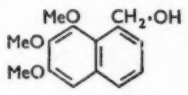
Aqueous-alcoholic solutions of tetra-*O*-methylpurpurogallin were irradiated in Pyrex tubes initially with a mercury vapour lamp. Ultraviolet spectroscopic data indicated that much starting material remained even after 165 hours. This suggested that, since the tropolone methyl ether absorbs strongly and over a wide range of frequencies in the near ultraviolet region, the use of sunlight might be more efficacious. When dilute solutions of the ether (III) were exposed to quite moderate sunlight under nitrogen, spectroscopic evidence indicated that no starting material remained after 2—3 weeks.

The residues from the methylene chloride extracts of these solutions were chromatographed. The first fractions afforded a colourless crystalline material, m. p. 81—82°. Elemental analysis and a methoxyl determination show that it is a photo-isomer of the ether (III). Its ultraviolet spectrum (see Figure) closely resembles that of the final irradiated solution and differs from that of the starting material. Its infrared spectrum showed a single band in the carbonyl region at 1748 cm.$^{-1}$, which suggested a saturated five-ring ketone and was consistent with one of our possible products (IV). We were not, however, able to obtain any carbonyl derivatives even under forcing conditions, and the compound was unaffected by sodium borohydride. It absorbed 2 mols. of hydrogen catalytically, but no crystalline product could be isolated; the infrared spectrum of the

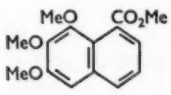
[1] Chapman and Pasto, *J. Amer. Chem. Soc.*, 1958, **80**, 6685.
[2] Grewe and Wulf, *Chem. Ber.*, 1951, **84**, 621.
[3] Forbes, *J.*, 1955, 3864.
[4] Gardner, Brandon, and Haynes, *J. Amer. Chem. Soc.*, 1957, **79**, 6334.

crude product differed appreciably from that of the starting material in the finger-print region, but the " carbonyl " band remained unaltered at 1748 cm.$^{-1}$. The photo-isomer in carbon tetrachloride slowly absorbed 2 mols. of bromine. The compound was recovered unchanged after 3 hours' boiling with alcoholic potassium hydroxide though the sequel shows that it is in fact an ester.

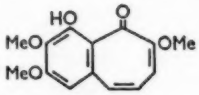
Structure (IV) implies considerable steric hindrance to reactions at the carbonyl centre and could be consistent with our findings in this respect. Reaction with lithium aluminium hydride would, however, be expected and could lead to the naphthalene (V) *via* an intermediate aldehyde. The alcohol (V) could well be obtained from the known



(V)

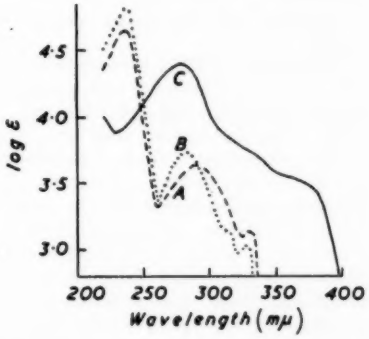


(VI)



(VII)

ester (VI) which had been synthesised by Haworth, Moore, and Pauson.[5] This ester (VI) has m. p. 80—81° practically identical with that of our photo-isomer. The two compounds were shown to be identical when we prepared the ester from tri-*O*-methylpurpurogallin (VII);[5] and they yielded the same product on reduction with lithium aluminium



Light absorption in ethanol of (A) methyl 6,7,8-trimethoxy-1-naphthoate, (B) 1-hydroxymethyl-6,7,8-trimethoxynaphthalene, and (C) tetra-O-methylpurpurogallin.

hydride. The structure of this compound (V) was established by its elemental analysis, methoxyl determination, the presence of a band at 3600 cm.$^{-1}$ (hydroxyl) and the absence of a band in the carbonyl region of the infrared spectrum.

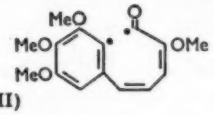
The structure (VI) accounts also for the " carbonyl " band at 1748 cm.$^{-1}$. Steric hindrance between the ester and the *peri*-methoxyl group forces the ester group out of the plane of the ring so that it is hardly conjugated with the ring. Its infrared absorption will thus be typical of a saturated rather than a phenyl-conjugated ester. This steric effect accounts also for the close similarity between the ultraviolet spectra of the ester (VI) and the alcohol (V) (see Figure). The unusual resistance of the ester to hydrolysis has already been described by Haworth *et al.*[5]

In our preparation of the ester (VI) from tri-*O*-methylpurpurogallin (VII), the rearrangement of the tropolone is carried out in ethylene glycol, rather than in ethanol in a sealed tube.[5] This is more convenient but the yield is not increased. Our attempts to convert the tropolone (III) directly into the ester (VI), with sodium methoxide in methanol, gave only the trimethyl ether (VII). The stability of this tropolone (III) towards alkali was demonstrated when some of it was recovered after treatment with alcoholic potassium hydroxide. This experiment gave also 6,7,8-trimethoxy-1-naphthoic acid.

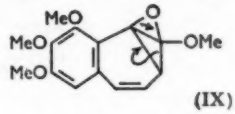
[5] Haworth, Moore, and Pauson, *J.*, 1949, 3271.

XUM

Since the methyl ester (VI) is unaccompanied by the analogous ethyl ester although ethanol is present in great excess, the photochemical transformation must be intramolecular. This contrasts with the ionic conversion of tropolones into benzenoid compounds which is intermolecular.[6] The intramolecular reaction appears to be unique and has two possible courses. The first involves initial fission of the tropolone ring to a diradical (VIII). Cyclisation to a six-membered ring and migration of the methoxyl group complete the process. The second and perhaps more likely course would involve the formation of a high-energy intermediate such as (IX) followed by a rearrangement of electrons. Fission of the tropolone ring as such and migration of a methoxyl group are not involved. Moreover, by this mechanism $C_{(2)}$ of the tropolone ring is displaced, whereas by the first



(VIII)



(IX)

mechanism $C_{(1)}$ is displaced to form the side-chain. This point will be settled by isotopic carbon studies. Other products of the reaction are being examined, also the influence of solvents on the course of the reaction.

Experimental

Infrared and ultraviolet spectra were measured respectively in carbon disulphide and ethanol.

Irradiation of Tetra-O-methylpurpurogallin.—(a) *By use of a mercury-vapour lamp* (Hanovia UVS 500). A solution of tetra-*O*-methylpurpurogallin [7] (100 mg.) in 20% v/v aqueous ethanol (50 c.c.) was irradiated under nitrogen. The ultraviolet spectrum of the solution was measured at intervals, and showed that much starting material remained after 165 hr.

(b) *In sunlight.* Tetra-*O*-methylpurpurogallin, m. p. 93—94° (3·0 g.), was dissolved in a mixture of oxygen-free water (700 c.c.) and ethanol (300 c.c.). The warmed solution (*ca.* 50°) was sealed up in a long glass tube under nitrogen. After 28 days' exposure to moderate summer sunlight the clear solution (which had darkened somewhat) was extracted with methylene chloride (3 × 200 c.c.). The combined extracts were dried rigorously ($MgSO_4$) and evaporated under reduced pressure (at *ca.* 25°). The residual gum (2·9 g.), which did not crystallise, was chromatographed in dry benzene on neutral alumina (Brockmann III—IV). Eluting the column with benzene gave 7 fractions (total 1·42 g.). Further elution with benzene containing 2% of methanol gave only a non-crystalline solid.

When boiled with light petroleum (b. p. 40—60°), fraction 1 gave a solid which on recrystallisation from light petroleum (charcoal) afforded colourless prisms of methyl 6,7,8-trimethoxy-1-naphthoate, m. p. 81—82° (Found: C, 65·4; H, 6·1; OMe, 44·3. Calc. for $C_{15}H_{16}O_5$: C, 65·2; H, 5·8; 4OMe, 44·9%), $\lambda_{max.}$ 238 and 290 mμ, (ε 45,660 and 4560 respectively), $\nu_{max.}$ 1748 cm.$^{-1}$. The compound showed no m. p. depression on admixture with an authentic specimen.

Fractions 2—7 were combined and again chromatographed on neutral alumina with benzene as eluent, giving (*a*) a further quantity of the photo-isomer (total 0·45 g., 15%, of pure material), (*b*) an amorphous compound (CO band at 1710 cm.$^{-1}$), and (*c*) a non-crystalline solid which appears to be polymeric.

1-*Hydroxymethyl*-6,7,8-*trimethoxynaphthalene* (V).—Methyl 6,7,8-trimethoxy-1-naphthoate (196 mg.) in dry ether (10 c.c.) was added to a cooled suspension of lithium aluminium hydride (200 mg.) in dry ether (10 c.c.). The mixture was heated under reflux for 2 hr., cooled, treated with water and dilute sulphuric acid, and extracted with ether. The extract was dried and evaporated, and the residue was chromatographed in dry benzene on neutral alumina (Brockmann III—IV). Elution with benzene gave 1-*hydroxymethyl*-6,7,8-*trimethoxynaphthalene* which crystallised from benzene–light petroleum in plates (95 mg.), m. p. 85—86° (Found: C, 67·7; H, 6·5; OMe, 37·2. $C_{14}H_{18}O_4$ requires C, 67·6; H, 6·5; OMe, 37·5%). The compound showed no m. p. depression on admixture with that obtained by reduction of the irradiation

[6] Pauson, *Chem. Rev.*, 1955, **55**, 1.
[7] Haworth, Moore, and Pauson, *J.*, 1948, 1045.

product with lithium aluminium hydride. Both specimens had $\nu_{max.}$ 3600 cm.$^{-1}$, $\lambda_{max.}$ 237 and 285 mμ (ε 64,870 and 6000 respectively).

Methyl 6,7,8-Trimethoxy-1-naphthoate.—Tri-*O*-methylpurpurogallin (Haworth *et al.*[6]) (3 g.) was heated with potassium hydroxide (5 g.) in ethylene glycol (45 c.c.) under nitrogen for 4 hr. at 160—170°, cooled, acidified with dilute hydrochloric acid, and extracted with ether. The extract was evaporated. A solution of the residue in 10% sodium hydroxide was warmed with methyl sulphate at 50° for 30 min. Next morning the slightly acidic solution was washed with 2N-sodium carbonate, dried, and evaporated to give a residue, which distilled at 165°/0·8 mm. A solution of the distillate in benzene was chromatographed on neutral alumina. Elution with benzene gave methyl 6,7,8-trimethoxy-1-naphthoate, prisms, m. p. 81—82° (from light petroleum).

When this experiment was conducted according to the directions of Haworth *et al.*[5], chromatography of the methylated product gave, in addition to the expected ester (VI), a second compound which crystallised from light petroleum in needles, m. p. 111—112°, depressed on admixture with the ester (VI) (Found: C, 67·6; H, 6·2; OMe, 37·4. $C_{16}H_{16}O_4$ requires C, 67·6; H, 6·5; 3OMe, 37·5%). Infrared and ultraviolet light absorption were almost identical with those of tetramethylpurpurogallin. M. p. behaviour established their non-identity.

6,7,8-Trimethoxy-1-naphthoic Acid.—Tetra-*O*-methylpurpurogallin (4·0 g.), potassium hydroxide (2·5 g.), and methanol (35 c.c.) were heated together in a sealed tube at 165° for 2·5 hr. Saturation of the cooled mixture with carbon dioxide gave a resin. The supernatant liquid was decanted, diluted with water, and extracted overnight with ether. Evaporation of the extract gave a solid (400 mg.) which was obtained crystalline from aqueous ethanol. One further crystallisation from benzene–cyclohexane afforded colourless needles of 6,7,8-trimethoxy-1-naphthoic acid, m. p. 146—147°. Haworth *et al.*[5] give m. p. 145—146°.

We thank Professor M. Stacey, F.R.S., for his interest and encouragement, also Messrs. Albright and Wilson for a grant (to R. A. R.).

CHEMISTRY DEPARTMENT, THE UNIVERSITY, BIRMINGHAM, 15. [*Received, March 12th,* 1959.]

---

557. *Hydride Ions in Organic Reactions. Part I. Dehydrogenation by Triphenylmethyl Perchlorate.*

By W. BONTHRONE and D. H. REID.

The use of triphenylmethyl perchlorate as a dehydrogenating agent has been investigated. Reaction is considered to proceed by successive elimination of a hydride ion and a proton, the key step being removal of the hydride ion. Necessary structural features in the substrate are discussed.

Application of the reagent in a new synthesis of perinaphthenylium salts is described.

CONSIDERABLE recent evidence shows that the key step in various organic oxidation–reductions involves transfer of hydrogen as hydride ion. These reactions include a number of dehydrogenations in which loss of two hydrogen atoms occurs, usually in two steps. The common, distinguishing feature of the general dehydrogenation is step (1) in which an electrophilic dehydrogenating agent (E^+) removes a hydride ion from the substrate (R_3CH). Subsequent loss of a proton from an acidic site in the resulting carbonium ion (R_3C^+) normally completes the dehydrogenation. Reaction may, however, not proceed beyond the initial step if the intermediate cation (R_3C^+) is very stable; this may indeed be capable of isolation as its salt (see below).

$$(1)\ R_3CH + E^+ \rightleftharpoons R_3C^+ + EH$$

$$(2)\ R_3C^+ \longrightarrow \text{Final product} + H^+$$

Reactions which proceed according to this mechanism include the following:

(*a*) Dehydrogenation of dihydro-aromatic compounds by quinones. This has been

the subject of detailed studies [1] by Braude and Linstead and their collaborators and finds use in preparative organic chemistry.

(*b*) Formation [2] of styrenes as intermediates in the Friedel–Crafts reactions of ethyl- and higher alkyl-benzenes with excess of acid chloride and aluminium chloride. Good evidence has been presented [3] that the dehydrogenating agent is the acylium cation present in excess. Under similar conditions certain derivatives of indane and tetralin are transformed into indenes and 1,2-dihydronaphthalenes, respectively.[4]

(*c*) Oxidation of alcohols to aldehydes or ketones, when dissolved in acidic systems capable of generating carbonium ions from the same or a different alcohol.[5] Thus acetone is formed from isopropyl alcohol in 50% sulphuric acid containing triphenylmethanol. Isotopic studies using labelled isopropyl alcohol proved that a hydride ion is transferred from the secondary alcohol to the triphenylmethyl cation formed by the action of sulphuric acid on triphenylmethanol. Related reactions which undoubtedly proceed by a similar mechanism include the oxidation of alcohols and ethers by tribiphenylylmethanol and sulphuric acid,[6] and of ethyl alcohol with xanthhydrol and hydrobromic acid [7] or with methoxytriphenylmethanols and hydrochloric acid.[8]

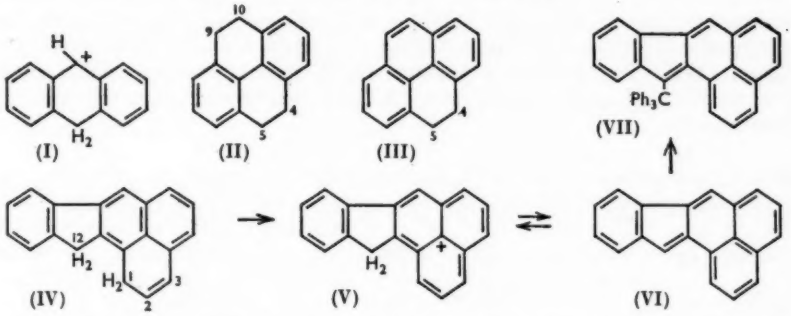
In the reactions considered under (*c*) the dehydrogenating agent, a carbonium ion, is first formed in the reaction system. In one case, that of the formation of tropylium salts by the action of triphenylmethyl salts on cycloheptatrienes,[9] a preformed carbonium ion has been used to remove the hydride ion. This process corresponds to the initial step (1) of the general dehydrogenation scheme given above. The possibility that preformed carbonium ions in the form of their salts might be used to dehydrogenate suitable substrates to relatively stable intermediate cations [step (1)] capable of further losing a proton with formation of a neutral product containing two fewer hydrogen atoms [step (2)] does not seem to have been considered. The work described in this paper is concerned with preliminary investigations on the general use of triphenylmethyl perchlorate as a dehydrogenating agent in this connection.

Triphenylmethyl perchlorate is most conveniently prepared by essentially the method of Hofmann and Kirmreuther [10] in which 70% perchloric acid is added to a solution of triphenylmethanol in acetic anhydride and acetic acid at room temperature. This procedure is conveniently adaptable to large-scale practice. The best dehydrogenation procedure consists in heating the substrate with triphenylmethyl perchlorate in boiling acetic acid for a time depending on the compound. Reaction is usually complete by the time the mixture has reached its reflux temperature and in no successful case was more than 15 minutes' boiling necessary. In several instances reaction was rapid at room temperature, but even then it was found expedient to raise the temperature of the mixture to the boiling point owing to the low solubility of triphenylmethyl perchlorate in cold acetic acid. In most cases clean products were readily obtained in high yield; this was not always so when acetonitrile and nitromethane were tried as solvents. Representatives from the following classes of compounds were chosen as substrates.

Hydrocarbons.—9,10-Dihydroanthracene was converted into anthracene in almost quantitative yield. The carbonium ion (I) is relatively stable, being a derivative of the diphenylmethyl cation.[11]

[1] Braude, Jackman, and Linstead, *J.*, 1954, 3548, 3564.
[2] Baddeley and Wrench, *J.*, 1956, 4943.
[3] Baddeley and Pickles, *J.*, 1953, 3726.
[4] Baddeley, Wrench, and Williamson, *ibid.*, p. 2110; *J.*, 1957, 2855.
[5] Bartlett and McCollum, *J. Amer. Chem. Soc.*, 1956, **78**, 1441.
[6] Schmidlin and Garcia-Banùs, *Ber.*, 1912, **45**, 3188.
[7] Fosse, *Compt. rend.*, 1901, **133**, 100, 881; Fosse and Bertrand, *ibid.*, 1904, **139**, 601.
[8] Kauffmann and Pannwitz, *Ber.*, 1912, **45**, 766.
[9] Dauben, Gadecki, Harmon, and Pearson, *J. Amer. Chem. Soc.*, 1957, **79**, 4557; Dauben and Honnen, *ibid.*, 1958, **80**, 5570.
[10] Hofmann and Kirmreuther, *Ber.*, 1909, **42**, 4856.
[11] Gold and Tye, *J.*, 1952, 2172.

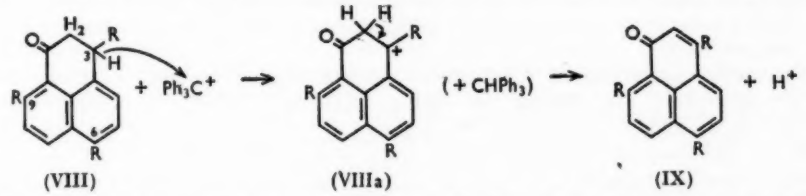
4,5:9,10-Tetrahydropyrene (II) might be expected to be dehydrogenated in two stages, first to 4,5-dihydropyrene (III) and thence to pyrene. On treatment with triphenylmethyl perchlorate it gave, however, pyrene as the main transformation product together with starting material, indicating that 4,5-dihydropyrene is dehydrogenated very much more rapidly than the tetrahydro-derivative (II).



1,12-Dihydroindeno[2,1-*a*]perinaphthene [12] (IV), in view of the unusually high stability [13] of the perinaphthenylium cation (XVIII; R = H), would be expected to give 12*H*-indeno[2,1-*a*]perinaphthenylium (V) as the intermediate carbonium ion, identical with the cation generated when indeno[2,1-*a*]perinaphthene (VI) dissolves in strong acids.[13a] Reaction occurred immediately at room temperature, to give indeno[2,1-*a*]perinaphthene (VI) as expected, together with its 12-triphenylmethyl derivative (VII) formed by subsequent rapid substitution. The two products were readily separated by extraction of their mixture in benzene with 77% (w/w) sulphuric acid in which the triphenylmethyl derivative is insoluble.

Ketones.—Results obtained on application of the reagent to cyclic ketones have persuaded us that dehydrogenation by triphenylmethyl perchlorate constitutes the best method for converting perinaphthanones into perinaphthenones.

Perinaphthan-1-one (VIII; R = H) and 3,6,9-trimethylperinaphthan-1-one (VIII; R = Me) gave perinaphthenone (IX; R = H) in 80% yield and 3,6,9-trimethylperinaphthenone (IX; R = Me) in 81% yield, respectively. The case of (VIII; R = Me) is noteworthy since all attempts [14] to prepare 3,6,9-trimethylperinaphthenone by oxidation of 1,4,7-trimethylperinaphthene (XVII; R = Me) (tautomeric with 3,6,9-trimethylperinaphthene) failed, as did attempts to dehydrogenate (VIII; R = Me) by other reagents. These failures were unexpected in view of the ease with which perinaphthene



(XVII; R = H) is oxidised to perinaphthenone [15] Loss of a hydride ion is considered to take place at $C_{(3)}$ of the perinaphthan-1-one nucleus (VIII) since a positive charge at

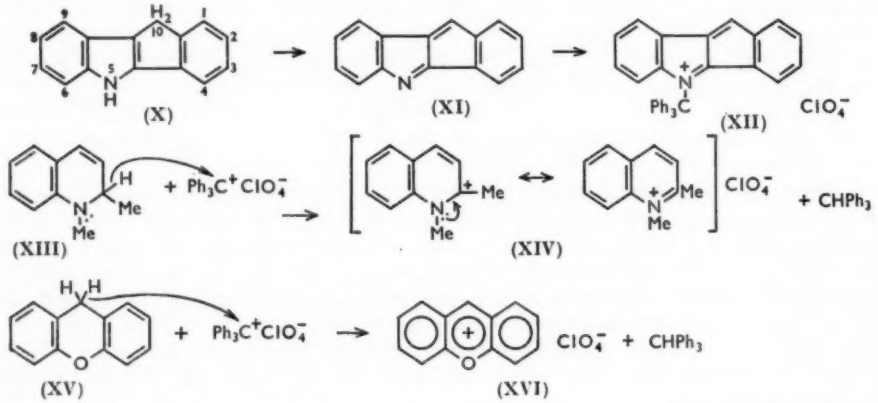
[12] Aitken and Reid, unpublished work.
[13] (*a*) Aitken and Reid, *J.*, 1956, 3487; (*b*) Reid, "Azulene and Related Substances," Chem. Soc. Special Publ. No. 12, 1958, p. 69; (*c*) Pettit, *Chem. and Ind.*, 1956, 1306; see also the synthesis described in this paper.
[14] Bonthrone and Reid, unpublished work.
[15] Lock and Gergely, *Ber.*, 1944, **77**, 461.

XUM

this site is resonance-stabilised by the adjacent aromatic nucleus. The considerable aromatic character of perinaphthenones provides the driving force for the subsequent loss of a proton from the intermediate cation (VIIIa).

Heterocycles.—5,10-Dihydroindolo[2,3-*a*]indene (X) was converted into a derivative of the hitherto unknown indeno[1,2-*b*]indole (XI). The dehydrogenation product (XI) itself was not isolated but was at once quaternised by the excess of reagent to give the 5-triphenylmethyl perchlorate (XII). This result seems surprising in view of the known lack of aromatic character of the corresponding carbocycle, 1,2:4,5-dibenzopentalene.[16]

Finally, 1,2-dihydro-1,2-dimethylquinoline (XIII) gave quinaldine methoperchlorate (XIV) in quantitative yield, and xanthen (XV) was readily converted into xanthylium perchlorate (XVI).



Discussion.—It is necessary to mention briefly the important factors upon which a successful dehydrogenation depends. These are implicit in the dehydrogenation scheme given at the beginning of this paper. For the initial step (1) they are (i) the electrophilic strength of the reagent E^+, (ii) the stability of EH, and (iii) the stability of the intermediate carbonium ion R_3C^+. The first two factors are constant for a given reagent and are henceforth ignored. The stability of the intermediate carbonium ion R_3C^+ is, then, all-important for a successful first step. For the final step (2) the acidity of the intermediate carbonium ion R_3C^+, determined by the relative stabilities of R_3C^+ and its conjugate base (the dehydrogenation product), is the decisive factor.

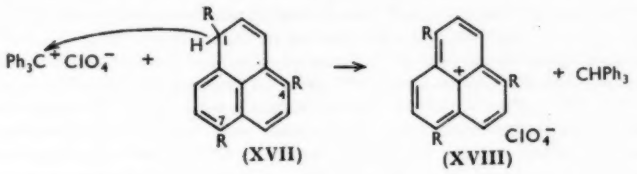
In the case of all successful dehydrogenations cited, except that of 5,10-dihydroindeno[1,2-*b*]indole, the substrate forms a stable carbonium ion (R_3C^+) as is readily envisaged. The driving force for the final step (2) is the additional resonance energy attending the loss of a proton.

The dehydrogenations of 1,2-dihydro-1,2-dimethylquinoline and xanthen require further discussion. The intermediate cations (XIV) and (XVI) cannot further lose a proton but are highly stabilised by participation of the 2*p*-electrons of the heteroatoms in the cyclical resonance and are themselves the final products. These reactions and the recently reported analogous preparation [9] of tropylium salts by abstraction of a hydride ion from cycloheptatrienes represent special cases of our general dehydrogenation scheme in which the intermediate carbonium ion (R_3C^+) is unusually stable.

These considerations, together with the known stability of the perinaphthenylium cation,[13] prompted us to attempt the synthesis of perinaphthenylium salts by allowing triphenylmethyl perchlorate and perinaphthenes to interact in acetic acid solution. Perinaphthene (XVII; R = H) gave perinaphthenylium perchlorate (XVIII; R = H)

[16] Blood and Linstead, *J.*, 1952, 2263.

smoothly in good yield as yellow needles which become bluish-green and finally black on exposure to the atmosphere, and are hydrolysed instantly in water to perinaphthene, perinaphthenone, and perchloric acid. In contrast, 1,4,7-trimethylperinaphthenylium perchlorate (XVIII; R = Me), prepared similarly from 1,4,7-trimethylperinaphthene



(XVII; R = Me), formed bronze-coloured needles, stable to the atmosphere, readily recrystallised from boiling acetic acid or acetonitrile without decomposition, and not readily solvolysed by water or alcohols.

We are now trying to elaborate this reaction into a convenient general preparation of perinaphthenylium salts. Other similar reactions will be reported later.

Experimental

M. p.s were determined on a Kofler-type heating stage. Chromatography was on activated alumina. Light petroleum was of boiling range 60—80° unless otherwise stated. Acetic acid was of " AnalaR " grade.

Dehydrogenation with Triphenylmethyl Perchlorate.—Stoicheiometric quantities of substrate and triphenylmethyl perchlorate were used unless otherwise indicated.

9,10-*Dihydroanthracene.* The hydrocarbon (180 mg.), triphenylmethyl perchlorate (343 mg.), and acetic acid (10 ml.) were boiled for 4 min. The cooled solution, whose colour had changed successively from deep yellow-green through deep green to very pale green, deposited anthracene (160 mg., 90%) as colourless plates, m. p. and mixed m. p. 215—218° (with sublimation).

4,5:9,10-*Tetrahydropyrene.* The hydrocarbon (1·03 g.; m. p. 132—135°), triphenylmethyl perchlorate (1·72 g.), and acetic acid (10 ml.) were boiled for 5 min., the initially deep yellow-brown and opaque solution becoming pale yellow and transparent. It was poured into water, and the mixture was extracted with light petroleum (2 × 300 ml.). The extracts were washed until free from acid and dried (K_2CO_3) before removal of the solvent, and the residual oil was dissolved in a hot mixture of ethanol (10 ml.) and benzene (8 ml.). Triphenylmethane (1·033 g., 89%), m. p. 92·5—94°, crystallised from the cooled solution. Benzene (2 ml.) was added to the mother-liquors, followed by picric acid (1·15 g.), and the mixture was boiled briefly to redissolve solid matter. Pyrene picrate (1·003 g., 93%; based on triphenylmethyl perchlorate used) crystallised from the cooled solution as orange-red needles, m. p. 222—224° (lit., m. p. 224°). After decomposition of the picrate (640 mg.) with dilute aqueous ammonia and working up in the usual manner, pyrene (190 mg., 62%) was obtained as colourless plates, m. p. and mixed m. p. 148—150°.

Dihydroindeno[2,1-a]*perinaphthene.* A solution of triphenylmethyl perchlorate (160 mg.) in acetic acid (40 ml.), at <20°, was added to a solution of dihydroindeno[2,1-*a*]perinaphthene (120 mg.) in acetic acid (40 ml.), also at <20°. The solution became red immediately and was left at room temperature for 3 hr. 12-*Triphenylmethylindeno*[2,1-a]*perinaphthene* (VII) separated from the solution as brown crystals (60 mg.), m. p. >320°, which dissolved in organic solvents to red solutions. Recrystallisation was from benzene (Found: C, 94·9; H, 4·7. $C_{39}H_{26}$ requires C, 94·7; H, 5·3%). It is insoluble in 77% (w/w) sulphuric acid.

The acetic acid mother-liquor was poured into water and extracted with benzene (300 ml.). The benzene extract was washed until free from acetic acid before being extracted with 77% (w/w) sulphuric acid (3 × 100 ml.). The acid extracts were washed with benzene (150 ml.) before dilution in water (2 l.), and the precipitated reddish-brown solid was taken up in ether (500 ml.). The ether solution was washed until free from acid with water and saturated sodium hydrogen carbonate solution before drying (K_2CO_3) and removal of solvent. The residue in benzene was filtered through a column (8 × 2·7 cm.) of alumina and the deep red eluates were evaporated to dryness. On addition of 1,3,5-trinitrobenzene to the residue

XUM

dissolved in absolute ethanol the trinitrobenzene complex of indeno[2,1-*a*]perinaphthene crystallised as black needles (25 mg.), m. p. and mixed m. p. with an authentic specimen [13a] 175—176°.

Perinaphthan-1-one. Triphenylmethyl perchlorate (686 mg.), perinaphthan-1-one (364 mg.), and acetic acid (30 ml.) were boiled for 10 min., or until dissolution was complete. The solution was poured into water (250 ml.), and the resulting emulsion was extracted with benzene (2 × 100 ml.). The benzene extracts were washed until free from acetic acid before extraction with concentrated hydrochloric acid (3 × 50 ml.). The acid extracts were washed once with benzene (50 ml.) before dilution in water (500 ml.). The precipitated solid was extracted with benzene (2 × 200 ml.). The combined benzene extracts were washed successively with water, saturated sodium hydrogen carbonate, and water, and dried (Na_2SO_4) before removal of solvent. The pale yellow residue, after sublimation at 150°/0·5 mm. followed by one crystallisation from light petroleum (b. p. 60—80°)–benzene (1 : 1), afforded perinaphthenone (IX; R = H) as yellow needles (290 mg., 80%), m. p. and mixed m. p. 155·5—156·5°.

The benzene solution from which perinaphthenone had been extracted by concentrated hydrochloric acid was washed successively with water, saturated sodium hydrogen carbonate solution, and water, and dried (Na_2SO_4) before removal of solvent. The residue crystallised from ethanol as colourless plates (300 mg., 62%), m. p. 93·5—94°, undepressed on admixture with triphenylmethane.

3,6,9-Trimethylperinaphthan-1-one. A mixture of 3,6,9-trimethylperinaphthan-1-one (448 mg.), triphenylmethyl perchlorate (686 mg.), and glacial acetic acid (50 ml.) was boiled for 15 min., then was worked up as described for the dehydrogenation of perinaphthan-1-one. After sublimation at 150°/0·1 mm. followed by one crystallisation from light petroleum (b. p. 60—80°) the crude product afforded *3,6,9-trimethylperinaphthen-1-one* (IX; R = Me) (360 mg., 81%) as yellow needles, m. p. 106—107° (Found: C, 86·6; H, 6·4. $C_{16}H_{14}O$ requires C, 86·4; H, 6·4%). Triphenylmethane (340 mg., 70%), m. p. 93—94°, was isolated from the original reaction mixture.

5,10-Dihydroindeno[1,2-b]indene. A boiling solution of triphenylmethyl perchlorate (185 mg.) in acetic acid (25 ml.) was added to one of 5,10-dihydroindolo[1,2-*a*]indene (110 mg.) in acetic acid (15 ml.), also at the b. p., the solution becoming blue. The solution was boiled for 1 min. and allowed to cool to room temperature. *5-Triphenylmethylindeno[1,2-b]indolium perchlorate* (XII) separated from the cooling solution as black crystals, m. p. >320° (Found: C, 73·6; H, 4·3; Cl, 5·8; N, 2·5. $C_{34}H_{24}O_4NCl$ requires C, 74·8; H, 4·4; Cl, 6·5; N, 2·6%), insoluble in benzene and non-polar solvents and dissolving in acetone or nitromethane to greenish-blue solutions.

1,2-Dihydro-1,2-dimethylquinoline. Triphenylmethyl perchlorate (343 mg.) was added to a solution of 1,2-dihydro-1,2-dimethylquinoline [17] (160 mg.) in acetic acid (6 ml.). The mixture was boiled for 1 min. during which a transient red colour developed and faded. The cooled solution deposited quinaldine methoperchlorate (XIV) (255 mg., 98%) as colourless prisms, m. p. and mixed m. p. 152—154°.

Xanthen. Xanthen (182 mg.), triphenylmethyl perchlorate (343 mg.), and acetic acid (10 ml.) were heated for 2 min. *Xanthylium perchlorate* (XVI) began to separate from the boiling solution as yellow plates. The product, filtered from the cooled solution, recrystallised from acetic acid as bronze plates (190 mg., 68%), m. p. (capillary) 225—226° to a red liquid (Found: C, 55·2; H, 3·3; Cl, 12·9. $C_{13}H_9O_4Cl$ requires C, 55·6; H, 3·2; Cl, 12·6%).

Preparation and Properties of Perinaphthenylium Perchlorate (XVIII; R = H).—A solution of triphenylmethyl perchlorate (686 mg.) in acetic acid (90 ml.) was added to one of perinaphthene (370 mg.) in acetic acid (10 ml.). Perinaphthenylium perchlorate began to separate from solution almost at once as yellow needles. After 5 min. it was filtered off, washed with anhydrous ether followed by dry light petroleum, and transferred immediately to a vacuum-desiccator. The perchlorate obtained (357 mg., 61%) was dried *in vacuo* for 5 hr. over phosphoric oxide and potassium hydroxide.

Owing to its instability to the atmosphere in which it blackens the perchlorate had to be analysed at once. Determination of the percentage of ClO_4 present was therefore carried out as follows: the dried perchlorate (357 mgm.) was hydrolysed with water (100 ml.), and the resulting yellow solid was filtered off through a sintered-glass funnel, with subsequent thorough washing with more water (100 ml.). The combined solutions containing perchloric acid were

[17] Bradley and Jeffrey, *J.*, 1954, 2770.

titrated against 0·05N-sodium hydroxide (Bromothymol Blue). A second determination was carried out on 328 mg. of perchlorate (Found: ClO_4, 37·2, 37·0. $C_{13}H_9O_4Cl$ requires ClO_4, 37·6%). *Perinaphthenylium perchlorate* is insoluble in non-polar solvents but dissolves readily in acetic acid, acetonitrile, and nitromethane, giving yellow solutions. It does not melt but decomposes slowly on heating.

The organic material filtered off after hydrolysis of the perchlorate (685 mg.) was dissolved in benzene (150 ml.) and extracted exhaustively with concentrated hydrochloric acid as described for the dehydrogenation of perinaphthan-1-one. The hydrochloric acid extracts thus gave perinaphthenone (180 mg., 39% based on perinaphthenylium perchlorate), m. p. 154—156°. The benzene solution from which perinaphthenone had been extracted with concentrated hydrochloric acid was washed in turn with water, saturated sodium hydrogen carbonate solution, and water before drying (Na_2SO_4) and evaporation of the solvent. The residual oil was taken up in light petroleum and purified through a column (15 × 2·8 cm.) of alumina, light petroleum being used as eluant. Solvent was evaporated from the colourless eluates (200 ml.), and the residual oil, dissolved in ethanol (30 ml.), was treated with 1,3,5-trinitrobenzene (110 mg.). The trinitrobenzene complex of perinaphthene crystallised as orange needles (150 mg., 15% based on perinaphthenylium perchlorate), m. p. 151—152° (decomp.), unchanged after recrystallisation from ethanol (lit.,[18] m. p. 159°). The perinaphthenone and perinaphthene thus isolated accounted for 54% of the perinaphthenylium perchlorate used in the experiment.

Preparation and Properties of 1,4,7-*Trimethylperinaphthenylium Perchlorate* (XVIII; R = Me).—Triphenylmethyl perchlorate (1·75 g.) in acetic acid (200 ml.) was added to a solution of 1,4,7-trimethylperinaphthene (1·06 g.) in acetic acid (20 ml.). 1,4,7-*Trimethylperinaphthenylium perchlorate* began to crystallise immediately from the resulting solution as yellow needles (570 mg., 37%). The salt, recrystallised from acetonitrile, was obtained as copper-coloured needles, decomp. >240° (Found: C, 63·3; H, 5·1; Cl, 11·1. $C_{16}H_{15}O_4Cl$ requires C, 62·7; H, 4·9; Cl, 11·6%). The compound is insoluble in non-polar organic solvents but in acetic acid or acetonitrile readily gives yellow solutions. It is stable to the atmosphere and is not readily solvolysed by water or alcohols.

DEPARTMENT OF CHEMISTRY, THE UNIVERSITY,
ST. ANDREWS, SCOTLAND.

[*Received, March 4th*, 1959.]

[18] Boekelheide and Larrabee, *J. Amer. Chem. Soc.*, 1950, **72**, 1245.

---

558. *The Preparation of Some 2-Amino- and 2-Phthalimido-benzophenones.*

By M. LAMCHEN and A. J. WICKEN.

Many substituted 2-phthalimidobenzophenones have been prepared by a Friedel–Crafts condensation of *o*-phthalimidobenzoic acid with substituted benzenes, and yields of approximately 70% were obtained in all cases where strongly electron-repelling groups were present; in absence of these groups yields were low.

When this method is inapplicable, the 2-phthalimidobenzophenones were obtained readily by fusion of the 2-aminobenzophenones with phthalic anhydride. The best general preparative method for 2-aminobenzophenones was that developed by Lothrup and Goodwin.

IN earlier communications [1,2] it was reported that, whereas 2,4-dimethoxy- and 4-methoxy-2′-phthalimidobenzophenones condensed with hydrazine to form substituted 1,2,4-triazacyclohepta-2,5,7-trienes, other 2-phthalimidobenzophenones underwent the normal Ing and Manske decomposition.[3] To investigate the effect of substituents on the reaction between hydrazine and 2-phthalimidobenzophenones, a number of 2-phthalimidobenzophenones were prepared.

The most obvious route seemed to be reaction of 2-aminobenzophenones with phthalic

[1] Engels, Lamchen, and Wicken, *Proc. Chem. Soc.*, 1958, 191.
[2] Engels, Lamchen, and Wicken, *J.*, 1959, 2694.
[3] Ing and Manske, *J.*, 1926, 2348.

XUM

anhydride, and we found that at 180—200° this gave good yields; the method is, however, limited by the availability of the 2-aminobenzophenones. The most exploited route [4] to 2-aminobenzophenones involves Friedel–Crafts condensation of a substituted toluene-*p*-sulphonylanthraniloyl chloride with benzene or a substituted benzene, followed by acid-hydrolysis: its disadvantage, when highly activating substituents are present, is the ease of sulphonation during hydrolysis. We have found that the phthaloyl group can be used to protect the amino-group, the 2-phthalimidobenzophenones being obtained directly and, if desired, these could usually be decomposed to give the corresponding 2-aminobenzophenones. In this manner we have prepared 4-methoxy-,[2] 2,4-dimethoxy-,[2] 4-methylthio-, and 2,4-dimethyl-2′-phthalimidobenzophenone. With aluminium chloride in tetrachloroethane, yields of 62—76% of purified material were obtained, except in the case of 2,4-dimethyl-2′-phthalimidobenzophenone where only a 22% yield was obtained. 2-Phthalimidobenzophenone itself was obtained in only 8% yield, indicating that the best results with this method are obtained when the benzene ring is activated by substituents. It is of interest that when a deactivating group is present, as in phthalanil, the condensation with 2-phthalimidobenzoyl chloride was completely unsuccessful; however, under the more vigorous conditions of boiling in nitrobenzene, phthalanil and 2-phthalimidobenzoyl chloride with zinc chloride in only catalytic quantities gave a yield of 17% of 2,4′-diphthalimidobenzophenone.

That this method is also applicable to the preparation of 3- and 4-phthalimidobenzophenones was shown by our preparation of 2,4-dimethoxy-3′- and -4′-phthalimidobenzophenone in the same high yields.[2] In a similar way 2-3′-nitrophthalimidobenzyol chloride with dimethylresorcinol gave 2,4-dimethoxy-2′-(3-nitrophthalimido)benzophenone.

In the preparation of 4-methoxy-2-phthalimidobenzophenone this method could not be used since during the condensation of phthalic anhydride with 4-methoxyanthranilic acid decarboxylation produced 3-phthalimidoanisole. Other cases where a Friedel–Crafts condensation could not give the benzophenone with substituents in the desired positions, *e.g.*, 2-methoxy-2′-phthalimidobenzophenone, were also encountered. Here the 2-aminobenzophenones had to be prepared first. For such cases we have found Lothrup and Goodwin's method [5] the most useful, namely, addition of phenylmagnesium bromide to acetanthranil at 0°, giving 2-acetamidobenzophenone which could be hydrolysed in good yield to 2-aminobenzophenone. We prepared similarly 2-amino-4-methoxy-, -2′-methoxy-, and -2′,4-dimethoxy-benzophenone and have converted them into the phthalimidobenzophenones by fusion with phthalic anhydride at 180—200°. In this method the substituent groups retain their positions and exert no orientating effect on the reaction as is found in a Friedel–Crafts reaction; the effect of substituent groups on the formation of the Grignard reagent is, however, a limitation, nitro-groups for instance completely preventing it.

Other known 2-aminobenzophenones, *e.g.*, 2-amino-2′-methyl-, -4′-methyl-, -4′-bromo-, and -4′-hydroxy-benzophenone, were similarly converted in good yield into the phthalimidobenzophenones by fusion with phthalic anhydride. 2-Aminoacetophenone gave 2-phthalimidoacetophenone.

The reaction of these substituted 2-phthalimidobenzophenones with hydrazine forms the basis of another paper.

Experimental

2-3′-Nitrophthalimidobenzoic Acid.—Equivalent quantities of anthranilic acid (10 g.) and 3-nitrophthalic anhydride (14·2 g.) were fused at 180—200° for 30 min. The crystalline product was recrystallised three times from glacial acetic acid to produce *2-3′-nitrophthalimidobenzoic acid* (16 g., 70%) as needles, m. p. 222—224° (Found: C, 57·6; H, 2·8; N, 9·1. $C_{15}H_8O_6N_2$ requires C, 57·8; H, 2·6; N, 9·0%).

2-Phthalimidobenzophenone.—*o*-Phthalimidobenzoic acid (20 g.) and phosphorus pentachloride (16 g.) were refluxed in dry, sulphur-free benzene (100 ml.) for 2 hr. After cooling,

[4] Cf. Simpson, Atkinson, Schofield, and Stephenson, *J.*, 1945, 646
[5] Lothrup and Goodwin, *J. Amer. Chem. Soc.*, 1943, **65**, 363.

powdered, anhydrous aluminium chloride (27 g.) was added in 30 min. An exothermic reaction produced a brownish-black complex. The mixture was left at room temperature for 1 hr., then refluxed for 1 hr. The complex was decomposed with ice and hydrochloric acid, and the excess of benzene removed by steam-distillation. The residual solid was filtered off and washed with dilute hydrochloric acid and then water. The solid was taken up in ether, and washed with dilute sodium hydroxide solution, then with water. The ether was dried and evaporated, to leave white crystals which were recrystallised from ethanol to yield 2-phthalimidobenzophenone (2 g., 8%) as needles, m. p. 198—199° (Engels, Lamchen, and Wicken [2] reported 199°).

2,4-*Dimethyl*-2′-*phthalimidobenzophenone*.—*o*-Phthalimidobenzoic acid (25 g.) was stirred with phosphorus pentachloride (20 g.) in dry redistilled *m*-xylene (100 ml.) for 1 hr. at 50—60°. To the cooled solution powdered anhydrous aluminium chloride (30 g.) was added in 30 min. The mixture was stirred at 80—90° for a further 4 hr., then worked up as above. The brown oil obtained on evaporation crystallised only when kept in the minimum amount of ether overnight at 0°; crystals were formed which then recrystallised from dilute ethanol to give 2,4-*dimethyl*-2′-*phthalimidobenzophenone* as rods (7 g., 22%), m. p. 172—175° (Found: C, 78·0; H, 5·0; N, 3·9. $C_{23}H_{17}O_3N$ requires C, 77·7; H, 4·8; N, 3·9%).

4-*Methylthio*-2′-*phthalimidobenzophenone*.—*o*-Phthalimidobenzoic acid (26·7 g.) was stirred vigorously with phosphorus pentachloride (21 g.) in dry *sym*-tetrachloroethane (100 ml.) for 2 hr. To the cooled solution, thioanisole (13 g.) was added, and then aluminium chloride (27 g.) in 30 min. The mixture was stirred at 40—50° for a further hour, decomposed, and steam-distilled as above. The residue, dissolved in benzene, was washed with 10% sodium carbonate and then water. The dried benzene solution on evaporation gave a solid residue, which recrystallised (charcoal) from acetic acid gave 4-*methylthio*-2′-*phthalimidobenzophenone* as rods (27 g., 73%), m. p. 192—195° (Found: C, 71·3; H, 4·05; N, 3·6; S, 8·5. $C_{22}H_{15}O_3NS$ requires C, 70·7; H, 4·05; N, 3·75; S, 8·6%).

2,4-*Dimethoxy*-2′-(3-*nitrophthalimido*)*benzophenone*.—Prepared as above from 2-3′-nitrophthalimidobenzoic acid (25 g.), phosphorus pentachloride (18 g.), *sym*-tetrachloroethane (100 ml.) (stirred for 2 hr. at 70°), dimethylresorcinol (15 g.), and aluminium chloride (25 g.), the purple complex was worked up in the same way as above. Distillation of the benzene gave a pale oil which solidified and on recrystallisation from glacial acetic acid yielded 2,4-*dimethoxy*-2′-(3-*nitrophthalimido*)*benzophenone* (6 g., 17%) as rectangular prisms, m. p. 248—250° (Found: C, 64·3; H, 3·65; N, 6·5. $C_{23}H_{16}O_7N_2$ requires C, 63·9; H, 3·7; N, 6·5%).

2,4′-*Diphthalimidobenzophenone*.—*o*-Phthalimidobenzoic acid (10 g.) was stirred with phosphorus pentachloride (8 g.) in anhydrous nitrobenzene (50 ml.) at 80° for 2 hr. Phthalanil (8·4 g.) and crushed anhydrous zinc chloride (1 g.) were added and the mixture refluxed for 6 hr. After cooling, the solution was made slightly alkaline with dilute aqueous sodium hydroxide, and the excess of nitrobenzene removed by steam-distillation. The black tarry residue was treated with charcoal in glacial acetic acid and from the filtered solution a light brown amorphous solid (5 g.) was slowly precipitated. Repeated recrystallisation from acetic acid yielded 2,4′-*diphtalimidobenzophenone* (3 g., 17%) as long white needles, m. p. 309—312° (Found: C, 73·3; H, 3·7; N, 5·8. $C_{29}H_{16}O_5N_2$ requires C, 73·7; H, 3·4; N, 5·9%).

m-*Phthalimidoanisole*.—4-Methoxyanthranilic acid (0·5 g.) and phthalic anhydride (0·45 g.) were refluxed in acetic acid (20 ml.) for 2 hr. The hot solution was poured into water (250 ml.), and the pale brown precipitate was recrystallised from dilute ethanol, to give m-*phthalimidoanisole* (0·53 g., 60%) as white needles, m. p. 123—124° (Found: C, 71·3; H, 4·4. $C_{15}H_{11}O_3N$ requires C, 71·2; H, 4·35%).

2-*Amino*-4-*methoxybenzophenone*.—Phenylmagnesium bromide, prepared from bromobenzene (14·1 g.) and magnesium (2·17 g.) in dry ether (200 ml.), was slowly added with stirring under strictly anhydrous conditions to an ice-cold suspension of 4-methoxyacetanthranil (17·5 g.) in dry benzene (200 ml.) during 30 min. The thick yellow suspension was stirred at room temperature for a further 30 min., the mixture then becoming too sticky for stirring. Hydrolysis of the complex with dilute hydrochloric acid was slow; it was allowed to proceed overnight, and completed by steam-distillation which also removed the solvents. The oily residue was ether-extracted and washed with dilute sodium hydroxide and water, then dried and evaporated to leave a thick oil. Without further purification this oil, presumably 2-acetamido-4-methoxybenzophenone, was hydrolysed by refluxing it with concentrated hydrochloric acid (20 ml.) and 96% ethanol (100 ml.) for 1 hr. This solution was then treated with charcoal, filtered, made alkaline with ammonia, diluted with water (200 ml.), and chilled in ice; a pale

XUM

yellow solid separated. Recrystallisation from dilute ethanol yielded *2-amino-4-methoxybenzophenone* (6·5 g., 32%) as pale yellow needles, m. p. 109—111° (Found: C, 73·9; H, 5·8; N, 6·0. $C_{14}H_{13}O_2N$ requires C, 74·0; H, 5·8; N, 6·2%).

The acidic aqueous solution, after ether-extraction, was made alkaline with ammonia and re-extracted with ether to yield another 0·5 g. of the compound.

2-Amino-2′-methoxybenzophenone.—A Grignard reagent was prepared from *o*-iodoanisole (29 g.) and excess of activated magnesium powder [6] (4 g.) in anhydrous ether (100 ml.). Unchanged magnesium was removed by filtration through glass wool. The ethereal solution was added slowly (30 min.) under anhydrous conditions to a stirred solution of acetanthranil (20 g.) in dry benzene (150 ml.) at 0°. A pale orange precipitate was formed almost immediately. The suspension was stirred for a further hour at room temperature and at 30° for a further 30 min. The mixture was worked up as above, to give the crude 2-acetamido-2′-methoxybenzophenone, which was then hydrolysed as above. After dilution, the solution was made alkaline with ammonia and ether-extracted. Evaporation of the ether gave 2-amino-2′-methoxybenzophenone (9 g., 32%), yellow plates (from dilute ethanol), m. p. 109—111° (Inagaki [7] reported m. p. 110—111° for the compound made by a different method).

2-Amino-2′,4-dimethoxybenzophenone.—This was prepared as 2-amino-2′-methoxybenzophenone, by using same quantities but with 4-methoxyacetanthranil (14 g.). After hydrolysis with alcoholic hydrochloric acid, the alcoholic solution was treated with charcoal, made alkaline with ammonia, diluted with water (200 ml.), and chilled in ice. An oil separated and slowly solidified. Recrystallisation from dilute ethanol yielded 2-amino-2′,4-dimethoxybenzophenone (5 g., 24%) as pale yellow rods, m. p. 119—121° (Found: C, 70·1; H, 6·0; N, 5·3. $C_{15}H_{15}O_3N$ requires C, 70·1; H, 5·85; N, 5·4%).

4-Methoxy-2-phthalimidobenzophenone.—2-Amino-4-methoxybenzophenone (4 g.) was fused with phthalic anhydride (2·6 g.) at 180—200° for 30 min. The clear melt obtained set to a glass on cooling, and recrystallisation from ethanol yielded *4-methoxy-2-phthalimidobenzophenone* (4 g., 64%) as rods, m. p. 143—145° (Found: C, 73·9; H, 4·5; N, 3·8. $C_{22}H_{15}O_4N$ requires C, 73·9; H, 4·2; N, 3·9%).

Similarly were prepared:

2-Methoxy-2′-phthalimidobenzophenone [6 g., 76%; from 2-amino-2′-methoxybenzophenone (5 g.) and phthalic anhydride (3·2 g.)], colourless rods (from acetic acid), m. p. 205—207° (Found: C, 74·0; H, 4·3; N, 3·8. $C_{22}H_{15}O_4N$ requires C, 73·9; H, 4·2; N, 3·9%).

2′,4-Dimethoxy-2-phthalimidobenzophenone [1·5 g., 67%; from 2-amino-2′,4-dimethoxybenzophenone (1·5 g.) and phthalic anhydride (0·86 g.)], rods (from dilute acetic acid), m. p. 175—177° (Found: C, 71·3; H, 4·6; N, 3·5. $C_{23}H_{17}O_5N$ requires C, 71·3; H, 4·4; N, 3·6%).

2-Methyl-2′-phthalimidobenzophenone [68%; from 2-amino-2′-methylbenzophenone [5] (5 g.) and phthalic anhydride (3·5 g.)], needles (from acetic acid), m. p. 185—188° (Found: C, 77·2; H, 4·3; N, 4·0. $C_{22}H_{15}O_3N$ requires C, 77·4; H, 4·4; N, 4·1%).

4-Methyl-2′-phthalimidobenzophenone (80%; from 2-amino-4′-methylbenzophenone [8] (3·5 g.) and phthalic anhydride (2·5 g.), 30 min.]. The light coloured glass obtained on cooling was recrystallised needles (from ethanol), m. p. 167—169° (Found: C, 78·1; H, 4·5; N, 4·05. $C_{22}H_{15}O_3N$ requires C, 77·4; H, 4·4; N, 4·1%).

4-Bromo-2′-phthalimidobenzophenone [77%; from 2-amino-4′-bromobenzophenone [9] (6 g.) and phthalic anhydride (3·2 g.), for 20 min.], diamond-shaped prisms (from acetic acid), m. p. 212—215° (Found: C, 61·9; H, 3·0; N, 3·6; Br, 19·8. $C_{21}H_{12}O_3NBr$ requires C, 62·1; H, 3·0; N, 3·45; Br, 19·7%).

4-Hydroxy-2′-phthalimidobenzophenone [78%; from 2-amino-4′-hydroxybenzophenone [10] (6·5 g.) and phthalic anhydride (4·5 g.), for 20 min.], plates (from acetic acid), m. p. 233—235° (Found: C, 73·6; H, 3·9; N, 3·9. $C_{21}H_{13}O_4N$ requires C, 73·4; H, 3·8; N, 4·1%).

2-Phthalimidoacetophenone [44%; from 2-aminoacetophenone [11] (6 g.) and phthalic anhydride (6·6 g.), 30 min.], plates (from dilute ethanol), m. p. 132—134° (Found: C, 72·7; H, 4·0; N, 5·2. $C_{16}H_{11}O_3N$ requires C, 72·5; H, 4·15; N, 5·3%).

UNIVERSITY OF CAPE TOWN, CAPE TOWN, SOUTH AFRICA. [*Received, March 2nd,* 1959.]

[6] Holliman and Mann, *J.*, 1942, 739.
[7] Inagaki, *J. Pharm. Soc. Japan*, 1939, **59**, 5.
[8] Scheifele and De Tar, *Org. Synth.*, 1952, **32**, 8.
[9] Miller and Backman, *J. Amer. Chem. Soc.*, 1935, **57**, 2443.
[10] Inagaki, *J. Pharm. Soc. Japan*, 1933, **53**, 686.
[11] Elson, Gibson, and Johnson, *J.*, 1930, 1131.

559. *Electrometric Titration of the Sodium Salts of Deoxyribonucleic Acids. Part VII.* The Reversible Dissociation at Low Temperatures.*

By A. R. Peacocke and B. N. Preston.

Dissociation curves in 0·05M-sodium chloride of herring-sperm sodium deoxyribonucleate have been studied at 0·3°, 0°, −0·4° and −0·75° by continuous titration. A reversible dissociation curve was obtained for the undenatured double-helical structure at the lowest temperature. Titration at 25° of nucleate which had undergone a full titration cycle at −0·75° gave anomalous dissociation curves identical with those of the untreated material. By comparison of the relative positions of the reversible titration curves of the non-hydrogen-bonded nucleate and of a mixture of equal amounts of this and of the original form, the validity of the method used for calculating the extent of denaturation from the displacement of titration curves was confirmed.

Earlier papers in this series reported studies of denaturation that occurs when neutral solutions of sodium deoxyribonucleate in the double-helical form are titrated to and from low or high pH. At 25° this goes to completion, the nucleate is irreversibly and completely disordered, and any hydrogen bonds that exist after this are regarded as randomly disposed. However, when the acid titration cycle was carried out at 0·4°, the resulting neutral nucleate solution, on undergoing a further acid titration cycle at 25°, exhibited "hysteresis" in its dissociation curves to the extent calculated for a sample still containing 60% of the nucleate in the double-helical form.[1] From this it was inferred that at 0·4° all the originally hydrogen-bonded groups may be ionised but that on removal of the protons with rise in pH, 60% of these re-formed in the original double-helical structure. Thus, it appeared that if titrations could be carried out at sufficiently low temperatures, it might be possible to observe a completely reversible dissociation curve for the double-helical structure which would be in its original form after undergoing this titration cycle. If this were so, it would confirm previous ideas and might afford useful means for following denaturation processes by means of changes in the *reversible* dissociation curves characteristic of the deoxyribonucleate molecule in the helical and the denatured states. Such reversible curves should avoid some of the ambiguities in titrations at 25° which arise when denaturation is concurrent with ionisation. This reversible dissociation curve of the double-helical structure had already been inferred [1] from those of the denatured nucleate and of the 40% denatured nucleate obtained in titration at 0·4°. We now describe titrations made below 0·4°, whereby the approach to reversibility was examined more closely. Reversible dissociation curves of the double-helical nucleate were observed at −0·75° and are compared below with those for the denatured molecule and for mixtures containing equal amounts of these two forms.

Experimental

Herring-sperm sodium deoxyribonucleate [2] (1·4 mg./ml.) in 0·05M-sodium chloride was titrated electrometrically with acid to about pH 2·7, then back-titrated with alkali. Continuous titration was made in a cell with liquid junction and a glass electrode, with the procedure and precautions already described.[2] The solutions of the "denatured" nucleate were obtained either by heating the sample at 100° for 20 min. in 0·05M-sodium chloride or by subjecting it to a titration cycle at 25° in the same solution.

The titration vessel was immersed in a brine-bath kept at 0·3°, 0°, −0·4°, or −0·75° ± 0·05°. The contents of the titration vessel were allowed to attain the temperature of the bath during

* Part VI, *J.*, 1958, 4117.

[1] Cox and Peacocke, *J.*, 1957, 4724.

[2] Cox and Peacocke, *J.*, 1956, 2499.

30 min. before the titration. No freezing occurred even at the lowest temperature (but some of the solutions were supercooled).

0·05M-Sodium borate and 0·05M-potassium hydrogen phthalate were used to calibrate the

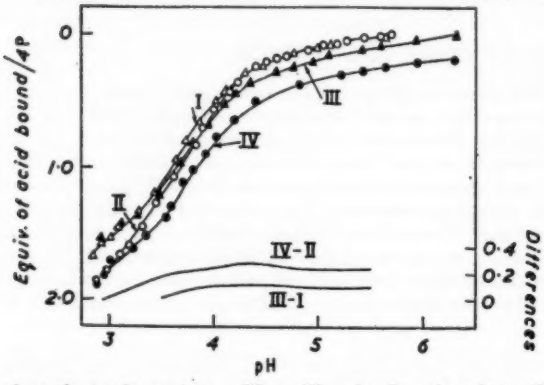


FIG. 1. *Titration curves of herring-sperm sodium deoxyribonucleate in 0·05M-sodium chloride at low temperatures.*

Upper figure: Left ordinate scale. I (△), *Forward-titration curve at* −0·4°. III (▲), *Back-titration curve at* −0·4°. II (○), *Forward-titration curve at* +0·3°. IV (●), *Back-titration curve at* +0·3°.

Lower figure: Right ordinate scale. Difference curves.

glass-electrode system. The pH value [3] assigned to the phthalate solution over the temperature range used was 4·008 and the interpolated value [4] given to the borate solution was 9·39 ± 0·01 for the range +1° to −1°.

Results.—The titration behaviour at low temperatures is shown in Fig. 1 where curves I and II are the irreversible forward-titration curves at −0·4° and 0·3°, respectively, and III

FIG. 2. FIG. 3.

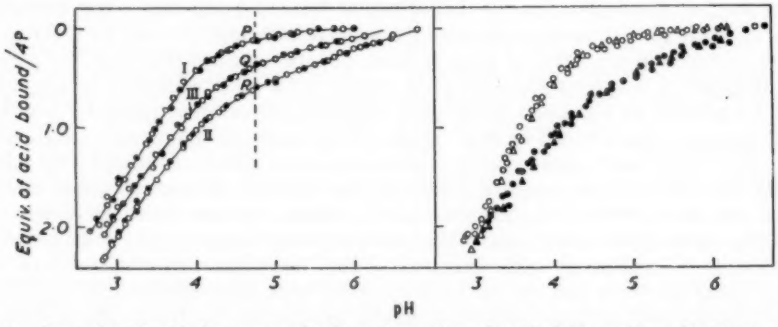


FIG. 2. *Reversible dissociation curves of sodium deoxyribonucleate in 0·05M-sodium chloride at* −0·75°. I, *Original untreated nucleate.* II, *Denatured nucleate.* III, *Mixture of* I *and* II *in equimolar proportion (on P basis).*

○ *Forward-titrations with acid.* ● *Back-titrations with alkali.* *P, Q, R, see text.*

FIG. 3. *Titration curve of sodium deoxyribonucleate at* 25° *in 0·05M-sodium chloride after a low-temperature titration cycle.*

○● *Forward- and back-titration curves of nucleate that has previously undergone a complete titration cycle at* −0·7° *in 0·05M-sodium chloride (several experiments).*

△▲ *Forward- and back-titration curves of the original untreated nucleate.*

and IV the corresponding reversible back-titration curves. Fig. 1 also gives a plot of the difference in acid bound between the forward- and back-titration curves for each of these temperatures and it can be seen that the difference was much less at the lower temperature. An intermediate pair of curves was also obtained at 0° but is omitted from Fig. 1 for clarity.

The reversible dissociation curve of the double-helical structure was observed when the temperature was reduced to −0·75° and is shown as curve I in Fig. 2. This reversibility suggested that at this temperature the nucleate had not become denatured and that the hydrogen

[3] Steinhardt and Harris, *J. Res. Nat. Bur. Stand.*, 1940, **24**, 335.
[4] Steinhardt, Fugitt, and Harris, *ibid.*, 1940, **25**, 519.

bonds had re-formed on back-titration. This was confirmed by submitting the neutral nucleate solution obtained by a complete titration cycle at −0·75°, to a further titration cycle at 25°; the points shown in Fig. 3 were then observed. Points on the forward- and back-titration curves of a previously untreated nucleate are also shown in Fig. 3 and it is apparent that the two sets of observations are coincident within experimental error. Thus the complete titration cycle at −0·75° had not permanently modified the dissociation behaviour of the various groups in the nucleate and it is reasonable to conclude that the double-helical structure remained intact since the curves of Fig. 3 are characteristic of this structure.

The reversible titration curve of the non-hydrogen-bonded nucleate at −0·75° was obtained by titrating, at this temperature, a neutral solution of nucleate which had been previously denatured either by heat or by acid-treatment. This curve, which is markedly different from the reversible curve of the hydrogen-bonded structure, is shown as II in Fig. 2.

Curve III in Fig. 2 is the reversible titration curve at −0·75° of a nucleate sample consisting of a mixture of equal amounts, with respect to nucleotide phosphorus, of untreated nucleate and of the denatured form. The ratio PQ/PR (Fig. 2), 0·54 ± 0·03, should represent [5] the proportion of the hydrogen bonds broken in the mixture, with no systematic variation according to the position of the point Q along III. Comparison of this value of 0·54 with the true value for this mixture of 0·50 indicates the limits of reliability of this type of computation from the dissociation curves of mixtures. This result supports the validity of the method used earlier in this series [5] for calculating the extent of denaturation from the displacement of titration curves.

Discussion

It has been shown that curve I (Fig. 2) obtained at −0·75° represents the reversible dissociation curve of the nucleate. As has been suggested earlier,[1] these observations can be interpreted in terms of the double-helical structure. It appears that at this low temperature the nucleate molecule retains its double-helical configuration in spite of the ionisation of the amino-groups and consequent disappearance of the hydrogen bonds. The highly specific structure of the molecule seems to be " frozen " into stability. This observation implies that, even for titrations carried out at 25°, ionisation of the amino-groups is a necessary but not sufficient condition for the loss of the double-helical structure. This accords with the mechanism of reversible dissociation which has been given previously [6] and which may be represented as:

$$\{\text{Helix}\}\text{-NH}_3^+ + (\text{-NH·CO-})\{\text{Helix}\} \rightleftharpoons \{\text{Helix}\}\text{-NH}_2 \ldots (\text{-NH·CO-})\{\text{Helix}\} + \text{H}^+$$

where $-NH_3^+$ and $-NH_2$ represent the charged and the uncharged form of the 1 : 6-amino-system capable of being hydrogen-bonded, although not necessarily defining the location of the proton; (-NH·CO-) is the system to which these groups are hydrogen-bonded in the double helix; the terms in the braces represent the configuration of the polynucleotide chains, and the dotted line represents the hydrogen bonds which link these systems.

The foregoing observations indicate that for permanent loss of the double-helical structure to occur (i) the hydrogen bonds must disappear as a result of ionisation and (ii) there must also be present enough thermal energy to cause rotation of the groups originally involved in hydrogen bonds. This rotation must attain the stage where there is a negligible chance of the double-helical form being recovered.

The results support an explanation, previously offered by one of us,[7] of some earlier observations on the effect of acid on sodium deoxyribonucleate. Reichmann, Bunce, and Doty [8] originally reported that light-scattering studies showed that the nucleate molecule collapsed on addition of acid to pH 2·6 in 0·2M-sodium chloride but that re-neutralisation of the solution to pH 6·5 restored the molecular size to its original value. Mathieson and

[5] Cox and Peacocke, *J.*, 1956, 2646.
[6] Cox and Peacocke, *J.*, 1958, 4117.
[7] Peacocke, *Chem. Soc. Special Publ.*, No. 8, 1957, p. 163; see also Shooter, *Progr. Biophysics Biophys. Chem.*, 1957, **8**, 327.
[8] Reichmann, Bunce, and Doty, *J. Polymer Sci.*, 1953, **10**, 109.

XUM

Matty [9] did not observe this restoration of the macromolecule to its original shape after re-neutralisation.

This apparent discrepancy can now be clearly attributed to the fact that in the work of Reichmann *et al.*[8] the acidification and re-neutralisation of the deoxyribonucleate were carried out in a cold room. The increased stability of the double-helical structure at these low temperatures and its reversible protonic dissociation under these conditions now explain the reversal in molecular shape and size which they observed. Mathieson and Matty's studies [9] were at 25° where the dissociation of the double-helical structure is irreversible, and thus no restoration of molecular shape is to be expected. Geiduschek [10] recently has reported light-scattering and viscosity measurements which support this explanation: whereas nucleate after acid-treatment at 25° has irreversibly collapsed, titration at 0° left the size and shape of the molecule unchanged.

The reversible dissociation curve of the fully denatured nucleate (II, Fig. 2) has been observed, and it is to be expected that partly denatured samples would give curves between I and II (Fig. 2). Curve III of Fig. 2 represents such a sample by being the reversible dissociation curve of a mixture of denatured and untreated nucleate. The position of such curves relative to I and II should allow determination of the extent and character of denaturation, regardless of the presence of such interfering effects as breaks in the main chain. This technique has been applied in a study of the denaturation of sodium deoxyribonucleate caused by γ-rays,[11] work on which will be more fully reported elsewhere.

The authors acknowledge gratefully the receipt of a maintenance grant from the Department of Scientific and Industrial Research (by B. N. P.).

DEPARTMENT OF MICROBIOLOGY,
THE UNIVERSITY, BIRMINGHAM, 15. [*Received, February* 18*th*, 1959.]

[9] Mathieson and Matty, *J. Polymer Sci.*, 1957, **23**, 747.
[10] Geiduschek, *ibid.*, 1958, **31**, 67.
[11] Peacocke and Preston, *J. Polymer Sci.*, 1958, **31**, 1.

---

560. *Steroids and Walden Inversion. Part XLIII.* The Bromination of* 3 : 5-cyclo*Steroids.*

By C. W. SHOPPEE, R. W. REES, G. H. R. SUMMERS, and (in part) G. D. PHILLIPS.

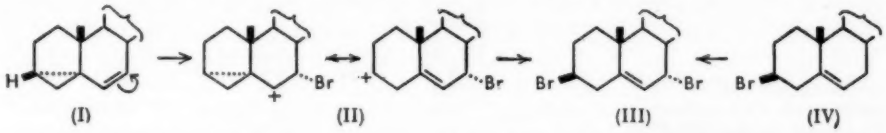
The reactions of 3 : 5-*cyclo*cholestane and the related 6-oxo-, 6-hydroxy-, and Δ^6-derivatives with bromine have been examined. The mechanism of the transformation of the epimeric 3 : 5-*cyclo*cholestan-6-ols into epimeric 3β : 5α : 6-tribromo-5α-cholestanes is discussed.

3 : 5-*cyclo*STEROIDS are unaffected by treatment with ozone [1] or perbenzoic acid [1,2] but readily react with hydrogen chloride, bromide, iodide,[1] or fluoride,[3] and with bromine.[1] The reactions of the epimeric 3 : 5-*cyclo*cholestan-6-ols with bromine have been used to assign configuration at $C_{(6)}$ in these alcohols and analogous compounds by Wagner, Wolff, and Wallis,[4] who thereby arrived at configurations opposite to those predicted by Dodson and Riegel,[5] assigned by Shoppee and Summers,[6] confirmed by Winstein and Kosower,[7]

* Part XLII, *J.*, 1959, 630.

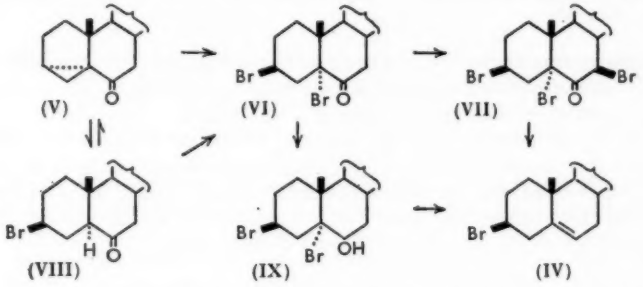
[1] Heilbron, Beynon, and Spring, *J.*, 1936, 907; 1937, 406, 1459.
[2] Wallis, Fernholz, and Gephart, *J. Amer. Chem. Soc.*, 1937, **59**, 137.
[3] Shoppee and Summers, *J.*, 1957, 4813.
[4] Wagner, Wolff, and Wallis, *J. Org. Chem.*, 1952, **17**, 529.
[5] Dodson and Riegel, *ibid.*, 1948, **13**, 424.
[6] Shoppee and Summers, *J.*, 1952, 3361.
[7] Winstein and Kosower, *J. Amer. Chem. Soc.*, 1956, **78**, 4347, 4354.

and later adopted by Smith and Wallis.[8] It seemed therefore desirable further to examine the reactions of 3 : 5-*cyclo*cholestane and some of its derivatives with bromine.



(I) (II) (III) (IV)

Although 3 : 5-*cyclo*cholestane undergoes electrophilic addition with hydrogen chloride,[9] bromide, and iodide,[10] to yield finally 3-methyl-A-norcholest-3-ene,[11] it does not react with bromine in ether at 15—36° (cf. ref. 10). It appears that the σ-electrons of the 3 : 5-bond require activation by an electron-attracting centre [12] or group at position 2 or 6. Thus 3 : 5-*cyclo*cholest-6-ene (I) with 1 mol. of bromine in ether at 0° readily gives 3β : 7α-



dibromocholest-5-ene [13] (III), also obtained from cholesteryl bromide (IV) by treatment with *N*-bromosuccinimide.[14] We regard the reaction as an electrophilic addition initiated by α-attack at $C_{(7)}$, and proceeding by way of the mesomeric cation (II) (alternatively envisaged as a 6-carbonium bromide intimate ion-pair which collapses by internal return) to yield the more thermodynamically stable product (III).

3 : 5-*cyclo*Cholestan-6-one (V) with bromine in pentane solution at 0° slowly gives 3β : 5α-dibromocholestan-6-one (VI). This transannular addition recalls the reaction of 3 : 5-*cyclo*cholestan-6-one with the four halogen acids to furnish the 3β-halogeno-5α-cholestan-6-ones,[3,15] and is clearly due to the activating influence of the adjacent carbonyl group; electrophilic attack at position 5 yields a cation, to be represented as a carbonium ion with configuration preserved at $C_{(3)}$, or as a 3α : 5α-bromonium ion, which is attacked by a bromide ion with inversion at $C_{(3)}$. 3 : 5-*cyclo*Cholestan-6-one (V) with 2 mols. of bromine in ether at 0°, dioxan at 15°, or acetic acid at 60°, gives the dibromo-ketone (VI) accompanied by 3β : 5α : 7β-tribromocholestan-6-one (VII); bromination of the dibromo-ketone (VI) in ether at 15° or in ether–acetic acid at ~40° also yields this tribromo-ketone (VII).

The 3β-configuration of the dibromo-ketone (VI) is established by its preparation by bromination of 3β-bromo-5α-cholestan-6-one [15] (VIII), and by its reduction with sodium borohydride to the 6-epimeric dibromohydrins represented by (IX), which on treatment with zinc in acetic acid eliminate hypobromous acid [16] to give cholesteryl bromide (IV).

[8] Smith and Wallis, *J. Org. Chem.*, 1954, **19**, 1628.
[9] Schmid and Kägi, *Helv. Chim. Acta*, 1950, **33**, 1582.
[10] Riegel, Hager, and Zenitz, *J. Amer. Chem. Soc.*, 1946, **68**, 2562; 1948, **70**, 887.
[11] Shoppee and Summers, *J.*, 1952, 2528.
[12] Kosower, *J. Amer. Chem. Soc.*, 1958, **80**, 3266.
[13] Bide, Henbest, Jones, and Peevers, *J.*, 1948, 1783.
[14] Bernstein, Sax, and Subbarow, *J. Org. Chem.*, 1948, **13**, 837.
[15] Ford and Wallis, *J. Amer. Chem. Soc.*, 1937, **59**, 1415; cf. Shoppee and Summers, *J.*, 1952, 1786.
[16] James, Rees, and Shoppee, *J.*, 1955, 1370 and references cited therein.

XUM

The polybromo-ketones (VI), (VII) were unchanged by treatment with sodium iodide in acetone, but by reduction with zinc in acetic acid gave cholestan-6-one.

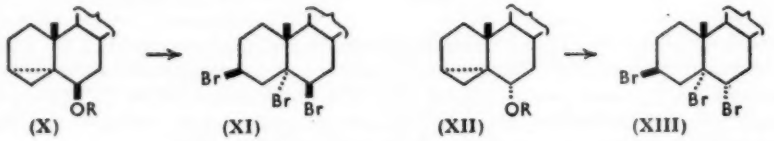
TABLE 1.

	CO : $\nu_{max.}$ (cm.$^{-1}$)	$\Delta\nu_{max.}$	$\lambda_{max.}$ (mμ)	Δλ	log ε	Δ log ε
5α-Cholestan-6-one	1711	—	280	—	1·6	—
3β-Bromo-5α-cholestan-6-one	1711	0	280	—	1·6	—
3β-Acetoxy-5α-cholestan-6-one [a]	1711	0	280	—	1·6	—
5α-Bromocholestan-6-one	1712	+1	308	+28	2·1	+0·5
3α : 5α-Dibromocholestan-6-one	1709	−2	308	+28	2·1	+0·5
3β : 5α-Dibromocholestan-6-one (VI)	1708	−3	309	+29	2·2	+0·6
3β-Acetoxy-5α-bromocholestan-6-one [a]	1711	0	308	+28	2·1	+0·5
3β : 5α : 7β-Tribromocholestan-6-one (VII)	1727	+16	306	+26	2·1	+0·5
3β-Acetoxy-5α : 7β-dibromocholestan-6-one [a,b]	1727	+16	305	+25	2·1	+0·5
3β-Acetoxy-5α : 7α-dibromocholestan-6-one [a,b]	1708	−3	340	+60	2·2	+0·6

[a] Cookson, *J.*, 1954, 282; Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175. [b] Cookson and Dandegaonker, *J.*, 1955, 352.

The α-configuration of the 5-bromine atom in the ketones (VI) and (VII) follows from their infrared and ultraviolet spectra, the essential features of which are recorded, with those of analogues of established configuration, in Table 1.

It will also be seen from the Table that the 7-bromine atom in the tribromo-ketone (VII) possesses the β-configuration. It is probable that bromination in acetic acid of the dibromo-ketone (VI) affords, by kinetic control, initially the 3β : 5α : 7α-tribromo-ketone, which by acid-catalysed enolisation,[17] or by reduction with hydrogen bromide and rebromination,[18] gives the 3β : 5α : 7β-tribromo-ketone (VII).



(X) (XI) (XII) (XIII)

M. p. 112° [−49°],[1] [−49·6°],[4] [−51·5°].[23] M. p. 160° (decomp.) [−50°] [4]

3 : 5-*cyclo*Cholestan-6β-ol (formerly " *i*-cholesterol "), its ethers, and its acetate (X; R = H, Me, Et, CH_2Ph, Ac) with bromine in anhydrous solvents at 0—15° give 3β : 5α : 6β-tribromocholestane (XI) in almost quantitative yield.[1] The alcohol and its methyl ether react thus in the presence of potassium acetate,[1] but we have observed that the bromination of the acetate is inhibited by potassium acetate. The structure of the tribromide (XI) follows from its preparation from cholesteryl bromide (IV) and bromine,[19] its 5α : 6β-configuration has been made virtually certain by Barton and Miller,[20] and is consistent with its stability to dehydrobromination by pyridine,* demonstrated by Wagner *et al.*[4] and confirmed by us.

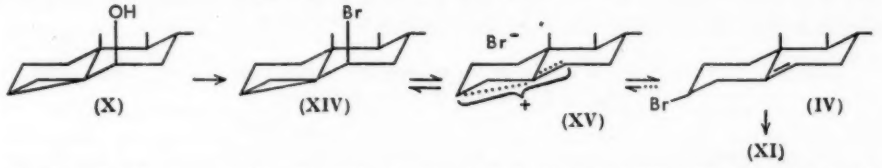
To gain insight into the mechanism of the bromination whereby 3 : 5-*cyclo*cholestan-6β-ol and its derivatives (X; R = H, Me, Ac) give 3β : 5α : 6β-tribromocholestane (XI), we have used a deficit of bromine (<2 mols.) combined with product analysis. With bromine (1 mol.) in anhydrous 1% ethereal solution at 0°, the 3 : 5-*cyclo*-6β-alcohol (X; R = H) affords a mixture, which cannot be separated chromatographically, of cholesteryl bromide (IV) and the 3β : 5α : 6β-tribromide (XI). Similarly, 3 : 5-*cyclo*cholestan-6β-yl methyl ether (X; R = Me) with bromine (1 mol.) in pentane at 0° slowly yields cholesteryl

* It may be noted that 4β-H and 5α-Br, although stereoelectronically suitably disposed (*trans*, diaxial), do not suffer elimination.[20]

[17] Corey, *J. Amer. Chem. Soc.*, 1954, **76**, 175.
[18] Cookson and Dandegaonker, *J.*, 1955, 352; James and Shoppee, *J.*, 1956, 1064.
[19] Kolm, *Monatsh.*, 1912, **33**, 447.
[20] Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 1066.

bromide and unchanged starting material; an attempt to follow the reaction kinetically failed because of the insufficient stability of solutions of bromine in pentane, whilst in carbon tetrachloride at 0° the reaction was too rapid. Finally, the 6β-acetate (X; R = Ac) with bromine (1 mol.) in pentane or carbon tetrachloride at 0° yielded a mixture of cholesteryl bromide and the 3β : 5α : 6β-tribromide.

The transformation (X ⟶ XI) thus appears to involve cholesteryl bromide as an intermediate. We suggest that 3 : 5-*cyclo*cholestan-6β-ol (X) by an S_Ni mechanism (involving attack by a partially polarised bromine molecule on the 6-oxygen atom and subsequent alkyl–oxygen fission) with retention of configuration of $C_{(6)}$ gives 3 : 5-*cyclo*-cholestan-6β-yl bromide (XIV) which rearranges, or as the ion-pair (XV) collapses by internal return, under thermodynamic control to give cholesteryl bromide (IV); in the presence of available bromine this affords the 3β : 5α : 6β-tribromide (XI) by *trans*-diaxial addition. An exact analogy is provided by the elegant work of Winstein and Kosower [7]



who describe the preparation from the 3 : 5-*cyclo*cholestan-6β-ol (X) with thionyl chloride in ether at 0° of 3 : 5-*cyclo*cholestan-6β-yl chloride and its rearrangement to cholesteryl chloride. Kinetic control leads to attack on the mesomeric carbonium ion at $C_{(6)}$ with retention of configuration, whereas thermodynamic control leads to stereospecific β-attack at $C_{(3)}$; this has been shown to be true, not only for the formation and rearrangement of 3 : 5-*cyclo*cholestan-6β-yl chloride, but also for its solvolysis in the absence and in the presence of lithium acetate in 90% dioxan at 25°. It is difficult to resist the conclusion that 3 : 5-*cyclo*cholestan-6β-yl bromide would show closely similar behaviour.

Wagner, Wolff, and Wallis [4] have reported that 3 : 5-*cyclo*cholestan-6α-ol (XII) with excess of bromine (3·6 mols.) in anhydrous 1% ethereal solution at 15° gave an 18% yield of 3β : 5α : 6α-tribromocholestane (XIII). In certain runs difficulty was encountered in the isolation of this compound in pure form because of its instability, whilst chromatographic methods were unsuccessful because of decomposition on the column. The compound was debrominated with sodium iodide in acetone to cholesteryl bromide more slowly than 3β : 5α : 6β-tribromocholestane (XI), whilst with pyridine at 15° it gave an unidentified product, m. p. 141°, $[\alpha]_D$ −22°, which although not analysed was stated to arise by loss of hydrogen bromide. In order to account for the production of the epimeric tribromides (XI, XIII) Wallis and his collaborators assumed a mechanism involving S_N2 replacement of the 6-hydroxyl group by a bromine anion with inversion, followed by transannular addition of bromine, and reversed the accepted configurations at $C_{(6)}$ of the 3 : 5-*cyclo*cholestan-6-ols. This mechanism is improbable because it requires a bimolecular nucleophilic substitution by bromide anions in the presence of that uniformly electrophilic reagent, the bromine molecule. It cannot be correct because the configurations at position 6 of the 3 : 5-*cyclo*cholestanols are known with certainty.[6,7,21] Both the transformations (X ⟶ XI) and (XII ⟶ XIII) in fact involve retention of configuration at position 6, and the configurational argument based upon the structure of the tribromo-compound is invalid, even although the tribromo-compound possesses the structure (XIII).

An analogy for the production from 3 : 5-*cyclo*-6α-cholestanol (XII), in low yield and by an S_Ni mechanism, of a 6α-bromo-compound (cf. XIII) can be derived from the work of Winstein and Kosower,[7] who found that 3 : 5-*cyclo*cholestan-6α-ol (XII) with thionyl

[21] Evans and Summers, *J.*, 1957, 906; Schleyer, Trifan, and Bacskai, *J. Amer Chem. Soc.*, 1958, **80**, 6691.

chloride in ether at −78° gave mainly 3 : 5-*cyclo*cholestan-6β-yl chloride, but with indications of the formation of 10—15% of 3 : 5-*cyclo*cholestan-6α-yl chloride. Wagner *et al.*,[4] however, isolated no other product [expected on this analogy to be the very stable 3β : 5α : 6β-tribromo-compound (XI) *], and do not comment on the fate of the residual 80% of the starting material.

The debromination of 3β : 5α : 6α-tribromocholestane (XIII) by sodium iodide in acetone to cholesteryl bromide [4] (IV) is consistent with the structure assigned; the specific rotation is not. The 6-epimers (XI, XIII) have almost identical negative specific rotations, giving a molecular-rotation difference for the inversion of 6β-Br to 6α-Br of only a few units. In the absence of vicinal action the molecular rotatory contributions are $\Delta Br_{6\beta}$ − 163° and $\Delta Br_{6\alpha}$ + 135°,[22] giving a molecular rotation difference (6β-Br ⟶ 6α-Br) of 300 units; similarly, for chlorine $\Delta Cl_{6\beta} = -100°$ and $\Delta Cl_{6\alpha} = +92°$,[22] giving a difference (6β-Cl ⟶ 6α-Cl) of about 200°. In the presence of vicinal action $\Delta Br_{6\beta}$ increases largely (Table 2); the variation in $\Delta Br_{6\alpha}$ is unknown because the compound (XIII) is the only 5α : 6α-dibromo-5α-cholestane yet described.

TABLE 2. *Effect of vicinal action on the molecular-rotation contributions* $\Delta Hal_{6\alpha}$ *and* $\Delta Hal_{6\beta}$ *in* 5 : 6-*dihalogeno*-5α-*cholestanes.*

	3β-Substituent					
Basic structure	H	OH	OAc	OBz	Cl	Br
5α : 6α-Dibromocholestane						−304° (XIII)
5α : 6β-Dibromocholestane	−212°	−240°	−290°	−239°	−288°	−302° (XI)

Although it has not been isolated, 3β : 5 : 6α-tribromo-5β-cholestane is formed to the extent of 10% from 3β : 5 : 6β-tribromo-5α-cholestane in chloroform solution at 40°, and its specific rotation has been calculated to be +41·9°; [23] it might be expected to undergo debromination with sodium iodide in acetone to cholesteryl bromide more slowly (5β-Br/6α-Br; *eq*/*eq*) than the 3β : 5α : 6β-tribromide (XI; 5α-Br/6β-Br; *ax*/*ax*) (this is true for the 3β-chloro-analogues, and this fact was used in the preparation of 3β-chloro-5 : 6α-dibromo-5β-cholestane [23]), but its positive specific rotation appears to preclude possible identification with the Wallis tribromo-compound.

We have been unable to prepare the Wallis 3β : 5α : 6α-tribromide (XIII). 3 : 5-*cyclo*-Cholestan-6α-ol used for bromination could not be recrystallised (cf. ref. 7) but had the correct specific rotation (−79°); there seems no reason to doubt its authenticity and homogeneity, since reduction of 3 : 5-*cyclo*cholestan-6-one by lithium aluminium hydride to 3 : 5-*cyclo*cholestan-6α-ol has been shown to be almost completely stereospecific.[4,6,7] In our hands, under the conditions specified by Wagner *et al.*,[4] the sole product of bromination of 3 : 5-*cyclo*cholestan-6α-ol (XII), or its acetate or its non-crystalline methyl ether, has been 3β : 5 : 6β-tribromo-5α-cholestane (XI). Use of the basic solvent dioxan [24,15] as an alternative to ether,[29] and of *NN*-dimethylformamide, and employment of pyridine sulphate dibromide as brominating agent, afforded mixtures of cholesteryl bromide and 3β : 5 : 6β-tribromo-5α-cholestane (XI). 3 : 5-*cyclo*Cholestan-6α-ol (XII) with 1 mol. of bromine in ether at 20° gave, however, mainly cholesteryl bromide (57%), with a small quantity of 3β : 5 : 6β-tribromo-5α-cholestane (XI). Similarly, in hexane at 20° with 1·2 mols. of bromine, it gave cholesteryl bromide (69%), with only traces of the 3β : 5α : 6β-tribromide (XI). In pentane with 2·4 mols. of bromine, the product was, surprisingly, almost exclusively the 3β : 5α : 6β-tribromide (69%). It appears reasonable to conclude that the

* Professor E. S. Wallis has most kindly informed us (letter of October 24th, 1958) that on occasion some of the 3β : 5α : 6β-tribromide was also isolated on reaction of the 3 : 5-*cyclo*cholestan-6α-ol with bromine.

[22] Shoppee, Howden, and Lack, unpublished work.
[23] Barton and Head, *J.*, 1956, 932.
[24] Yanovskaya, Terent'ev, and Belenkit, *Zhur. obshchei Khim.*, 1952, **22**, 1594; Dombrovskit, *ibid.*, 1954, **24**, 610.

transformation (XII ⟶ XI), like the change (X ⟶ XI), involves cholesteryl bromide as an intermediate.

These negative results were communicated in 1953 to Professor E. S. Wallis, who suggested the possible importance of traces of moisture. If adventitious traces of water were present during bromination, hydrogen bromide would be generated in a self-sustaining reaction: $Br_2 + H_2O \rightleftharpoons HOBr + HBr \xrightarrow[ROH]{} RBr + H_2O$. Esterification by hydrogen bromide of the highly reactive pseudoallylic secondary alcohol (XII) by mechanism S_N2 or S_Ni (with stereospecific 6β-attack on the 3 : 5-*cyclo*-cation under kinetic control) would lead to 3 : 5-*cyclo*cholestan-6β-yl bromide, but by mechanism S_Ni under conditions inhibiting ionisation could proceed through a configuration-preserving rearrangement of a hydrogen-bonded complex $R\diagup^{OH}_{Br}\!\!>H$ to furnish 3 : 5-*cyclo*cholestan-6α-yl bromide. Even so, it is not clear how the Wallis 3β : 5α : 6α-tribromide (XIII) could arise, since all the evidence[4,6,7] indicates that 6α-substituted 3 : 5-*cyclo*steroids rearrange to 3β-substituted Δ^5-steroids, which according to the literature afford 5α : 6β-dibromides and not 5α : 6α-dibromides.

Experimental

For general directions see *J.*, 1959, 630. $[\alpha]_D$ refer to chloroform solutions; ultraviolet absorption spectra were measured for ethanol solutions on a Unicam S.P. 500 spectrophotometer with a corrected scale, and infrared absorption spectra were determined on a Grubb-Parsons double-beam grating instrument.

Attempted Bromination of 3 : 5-cyclo*Cholestane*.—3 : 5-*cyclo*Cholestane[6,9,27] (m. p. 77°; 300 mg.) in (*a*) ether at 20° for 24 hr., or ether–acetic acid (1 : 1) (*b*) at 0° for 2 hr. or (*c*) at 40° for 24 hr., was treated with an excess of bromine. In each case evaporation of the orange solution at 20°/10 mm. gave a nearly quantitative recovery of 3 : 5-*cyclo*cholestane, m. p. and mixed m. p. 74—76° (from acetone).

Bromination of 3 : 5-cyclo*Cholest-6-ene* (I).—3 : 5-*cyclo*Cholest-6-ene,[10] m. p. 73°, $[\alpha]_D$ −46° (*c* 1·0) (1 g.), in chloroform (5 c.c.) was treated with a solution of bromine (434 mg., 1 mol.) in chloroform (5 c.c.) at 0°. The colourless solution was evaporated at 20°/10 mm., and the residual oil (1·38 g.) crystallised from acetone to give 3β : 7α-dibromocholest-5-ene (III), m. p. 140—142°, which did not depress the m. p. of a specimen prepared from cholesteryl bromide and *N*-bromosuccinimide.[14]

Bromination of 3 : 5-cyclo*Cholestan-6-one* (V).—(*a*) 3 : 5-*cyclo*Cholestan-6-one (m. p. 97°) (1 g.) in pentane was treated with bromine (415 mg., 1 mol.) in pentane at 0° overnight. After removal of pentane at 20°/10 mm., the usual isolation procedure gave a colourless solid, which by recrystallisation from ether–methanol yielded 3β : 5-*dibromo-5α-cholestan-6-one* (VI) (690 mg.), m. p. 133—134°, $[\alpha]_D$ −121° (*c* 2·2), $\lambda_{max.}$ 309 mμ (log ε 2·2), $\nu_{max.}$ 1708 cm.$^{-1}$ [Found (after drying at 20°/0·02 mm. for 20 hr.): C, 59·1; H, 7·9; Br, 29·6. $C_{27}H_{44}OBr_2$ requires C, 59·5; H, 8·1; Br, 29·4%].

(*b*) The ketone (1 g.) in ether (15 c.c.) was treated with a 3·2% solution of bromine in ether (13 c.c., 1 mol.) at 0°. The colour was discharged immediately; the solution was kept overnight at 0°, and then worked up in the usual way to give an oil (1·38 g.), which solidified when stirred with pentane. The solid was extracted with boiling ether, and the ether-insoluble material recrystallised from dioxan, to yield 3β : 5 : 7β-*tribromo-5α-cholestan-6-one* (VII) (40 mg.), m. p. 190°, $[\alpha]_D$ −51° (*c* 2·0), $\lambda_{max.}$ 306 mμ (log ε 2·1), $\nu_{max.}$ 1727 cm.$^{-1}$ [Found (after drying at 20°/0·02 mm. for 20 hr.): C, 52·8; H, 7·0; Br, 40·5. $C_{27}H_{43}OBr_3$ requires C, 52·0; H, 6·95; Br, 38·5%]. Evaporation of the ethereal solution and recrystallisation of the resulting solid from ether–methanol gave the 3β : 5α-dibromo-ketone (VI) (281 mg.), m. p. and mixed m. p. 133—134°.

(*c*) The ketone (1 g.) in ether (15 c.c.) was similarly treated with a 3·2% solution of bromine in ether (26 c.c., 2 mol.) at 0°, to yield a product (1·60 g.) separated as above into the 3β : 5α : 7β-tribromo-ketone (VII) (370 mg.), m. p. 190°, and the 3β : 5α-dibromo-ketone (VI) (1·03 g.), m. p. 133°.

(*d*) The ketone (330 mg.) in dioxan (10 c.c.) was treated with a 2·2% solution of bromine in

[25] Chesterman, *J.*, 1935, 906.
[26] Buswell, Rodebush, and Roy, *J. Amer. Chem. Soc.*, 1938, **60**, 2528.
[27] Karrer and Schmid, *Helv. Chim. Acta*, 1949, **32**, 1371.

XUM

dioxan (10 c.c., 1·7 mol.) at 20° overnight, to yield a product separated as above into the 3β : 5α : 7β-tribromo-ketone (VII) (170 mg.), m. p. 190°, $[\alpha]_D$ −50° (*c* 1·0), and the 3β : 5α-dibromo-ketone (VI) (320 mg.), m. p. 133°, $[\alpha]_D$ −123° (*c* 1·0).

(*e*) The ketone (436 mg.) in acetic acid (10 c.c.) at 60° was treated with a 6% solution of bromine in acetic acid (5 c.c., 1·7 mol.) and boron trifluoride–ether complex (0·5 c.c.). After 15 min. at 60° and 1 hr. at 20°, the product yielded, by separation as above, the 3β : 5α : 7β-tribromo-ketone (VII) (91 mg.), m. p. 190°, and the 3β : 5α-dibromo-ketone (VI) (506 mg.), m. p. 133°.

Bromination of 3β : 5-*Dibromo-5α-cholestan-6-one* (VI).—(*a*) The 3β : 5α-dibromo-ketone (458 mg.) in ether was treated with a 3·1% solution of bromine in ether (13·4 c.c., 3 mol.) at 20° for 3 hr. to give, after separation as described above, the 3β : 5α : 7β-tribromo-ketone (VII) (80 mg.), m. p. and mixed m. p. 190° (from dioxan), and unchanged starting material, m. p. 133°.

(*b*) The 3β : 5α-dibromo-ketone (500 mg.) in 1 : 1 acetic acid–ether (5 c.c.) was treated with a 3·1% solution of bromine in acetic acid (4·6 c.c., 1 mol.) at 40° for 1 hr. and then stored overnight. The crystalline precipitate, after removal of ether at 20°/10 mm., was filtered off, washed with ether, and recrystallised from dioxan, to give the 3β : 5α : 7β-tribromo-ketone (VII) (150 mg.), m. p. and mixed m. p. 190—191°. Concentration of the filtrate and washings gave unchanged starting material (400 mg.), m. p. 133°.

Bromination of 3β-*Bromo-5α-cholestan-6-one* (VIII).—(*a*) 3β-Bromo-5α-cholestan-6-one,[15] m. p. 123°, $\lambda_{max.}$ 280 mμ (log ε 1·6), $\nu_{max.}$ 1711 cm.$^{-1}$ (200 mg.), in 2 : 1 acetic acid–ether (7 c.c.) was treated with a 15·6% solution of bromine in acetic acid (0·43 c.c., 1 mol.) at 0° overnight. Removal of ether in a vacuum produced a crystalline precipitate; filtration and recrystallisation from ether–methanol gave 3β : 5-dibromo-5α-cholestan-6-one (VI), m. p. and mixed m. p. 133—134°.

(*b*) The 3β-bromo-ketone (500 mg.) in 1 : 5 acetic acid–ether (6 c.c.) was treated with a 15·6% solution of bromine in acetic acid (1·1 c.c., 1 mol.) at 36°. The colour rapidly disappeared, and the solution was heated on a steam-bath for 0·5 hr. Evaporation at 20°/10 mm. gave crystals, which were collected and recrystallised from ether–methanol, to yield 3β : 5-dibromo-5α-cholestan-6-one, m. p. and mixed m. p. 133—134°, $[\alpha]_D$ −121° (*c* 1·0).

Reduction of 3β : 5-*Dibromo-5α-cholestan-6-one* (VI).–(*a*) The 3β : 5α-dibromo-ketone (190 mg.) was refluxed in methanol (20 c.c.) with sodium borohydride (150 mg.) for 1 hr. The usual isolation procedure furnished a mixture of the epimeric 3β : 5-dibromo-5α-cholestan-6-ols (190 mg.), which failed to crystallise and was heated with zinc dust (100 mg.) in acetic acid at 100° for 0·5 hr. The usual working up gave an oil (150 mg.), which was chromatographed on aluminium oxide (4 g.) in pentane; elution with pentane gave cholesteryl bromide (140 mg.), m. p. and mixed m. p. 96—98° (from acetone).

(*b*) The 3β : 5α-dibromo-ketone (68 mg.) in acetic acid was refluxed with zinc dust for 4 hr. The cooled solution was filtered, diluted, and extracted with pentane to yield, after working up, an oil (47 mg.) which soon crystallised and by recrystallisation from methanol yielded 5α-cholestan-6-one, m. p. and mixed m. p. 96°.

(*c*) The 3β : 5α-dibromo-ketone (214 mg.) failed to react with sodium iodide (400 mg.) in acetone (25 c.c.) at 20° during 18 hr. and was recovered unchanged (m. p. and mixed m. p. 133°).

Attempted Rearrangement of 3β : 5-*Dibromo-5α-cholestan-6-one* (VI).—The 3β : 5α-dibromo-ketone (200 mg.) in 19 : 1 acetic acid–ether (40 c.c.) was not rearranged by treatment with 48% hydrobromic acid (2 c.c.) at 20° during 18 hr. and was recovered (197 mg.) unchanged (m. p. and mixed m. p. 133°, after crystallisation from ether–methanol).

Reduction of 3β : 5 : 7β-*Tribromo-5α-cholestan-6-one* (VII).—(*a*) The 3β : 5α : 7β-tribromo-ketone (100 mg.) in acetic acid was refluxed with zinc dust for 4 hr. The product, isolated as under (*b*) above, was 5α-cholestan-6-one, m. p. and mixed m. p. 96°.

(*b*) The 3β : 5α : 7β-tribromo-ketone (317 mg.) failed to react with sodium iodide (600 mg.) in refluxing acetone during 2·5 hr., and was recovered unaltered (m. p. 188—190° after recrystallisation from dioxan).

Bromination of 3 : 5-cyclo*Cholestan-6β-ol and Derivatives* (X; R = H, Me, Ac).—(*a*) The alcohol, m. p. 73° (120 mg.), in ether (5 c.c.) with a 2% solution of bromine in ether (2·5 c.c., 1 mol.) at 0° overnight gave, after the usual isolation procedure, an oil, which was chromatographed on aluminium oxide (5 g.) in pentane. Elution with pentane yielded material which, after repeated recrystallisation from acetone, furnished cholesteryl bromide, m. p. and mixed m. p. 96°, whilst further elution with pentane gave material (82 mg.) which, after crystallisation

XUM

from ethanol–acetone, yielded 3β : 5 : 6β-tribromo-5α-cholestane, m. p. and mixed m. p. 112°. When the alcohol (146 mg.) was treated similarly with 2·3 mol. of bromine in ether, the sole product was 3β : 5 : 6β-tribromo-5α-cholestane (230 mg.), m. p. and mixed m. p. 111—112°, which crystallised readily from ethanol–acetone. A series of brominations of the alcohol with 2·3 mols. of bromine at room temperature for 24—48 hr. in pentane, chloroform, carbon tetrachloride, or acetic acid, gave uniformly almost quantitative yields of 3β : 5 : 6β-tribromo-5α-cholestane, m. p. and mixed m. p. 112° (from ethanol–acetone).

(*b*) The methyl ether, m. p. 79° (500 mg.), in pentane with a 1·6% solution of bromine in pentane (12·5 c.c., 1 mol.) at 0° overnight gave a pale yellow solution, which by the usual working up furnished an oil. This was moistened with acetone–methanol and set aside overnight at 0°, and the resulting solid was triturated with methanol, filtered off, and recrystallised from acetone–methanol to give cholesteryl bromide, m. p. and mixed m. p. 96—97° [Found (after drying at 15°/0·03 mm. for 20 hr.): C, 72·0; H, 10·3. Calc. for $C_{27}H_{45}Br$: C, 72·2; H, 10·1%]; concentration of the methanolic filtrate gave 3 : 5-*cyclo*cholestan-6β-yl methyl ether, m. p. and mixed m. p. 78—79°. The methyl ether (500 mg.) in carbon tetrachloride, similarly treated with 1 mol. of bromine in carbon tetrachloride, gave an oil which crystallised when stirred with acetone–methanol and kept at −80° for 8 hr. The solid material was filtered off, washed with cold acetone–methanol, and recrystallised from acetone, to give crystals, m. p. 102—103°, which appeared to consist of a mixture of cholesteryl bromide and 3β : 5 : 6β-tribromo-5α-cholestane [Found (after drying at 15°/0·03 mm. for 20 hr.): C, 66·7; H, 11·1%]. The acetone–methanol filtrate and washings, on concentration, gave crystals, which were recrystallised from methanol to give the methyl ether, m. p. 75—78°. The methyl ether (1 g.) was recovered unchanged (m. p. 76—78°) after being refluxed with *N*-bromosuccinimide (1 g.) in carbon tetrachloride (20 c.c.) for 0·5 hr.

(*c*) The acetate, m. p. 73° (150 mg.), in pentane with a 4% solution of bromine in pentane (3 c.c., 2·2 mol.) after 4 days at 0°, furnished by the usual isolation procedure an oil, which was chromatographed on neutralised aluminium oxide [27] (12 g.) in pentane. Elution with pentane gave material (43 mg.) which after repeated recrystallisation from acetone gave cholesteryl bromide, m. p. and mixed m. p. 96°, whilst further elution with pentane gave material (178 mg.), which after recrystallisation from acetone–methanol gave 3β : 5 : 6β-tribromo-5α-cholestane, m. p. and mixed m. p. 111—112°, $[\alpha]_D$ −48° (*c* 0·9). A similar bromination of the acetate (200 mg.) with 2·2 mols. of bromine in carbon tetrachloride (cf. ref. 12) at 0° for 24 hr. gave on chromatography and crystallisation 3β : 5 : 6β-tribromo-5α-cholestane (227 mg.), m. p. and mixed m. p. 111—112°, and cholesteryl bromide (21 mg.), m. p. and mixed m. p. 96°. A series of brominations of the acetate with 2·8 mols. of bromine in ether at 0° for 36 hr., in chloroform at 0° for 48 hr., and in acetic acid at 25° for 20 hr., gave almost quantitative yields of 3β : 5 : 6β-tribromo-5α-cholestane, m. p. and mixed m. p. 111—112°; in acetic acid in presence of anhydrous potassium acetate bromination did not occur during 3 days at 25° and 3 : 5-*cyclo*cholestan-6β-yl acetate, m. p. and mixed m. p. 73—74° (from acetone–methanol), was recovered.

Bromination of 3 : 5-cyclo*Cholestan-6α-ol and its Derivatives* (XII; R = H, Ac, Me).—The alcohol was prepared from 3 : 5-*cyclo*cholestan-6-one,[6] m. p. 97°, by reduction with lithium aluminium hydride;[4,6,7] the product solidified after drying at 0·02 mm. for 48 hr., but a seed was not available and could not be procured, and despite many attempts to crystallise the product from acetone or acetonitrile [7] experiments had to be carried out on the unrecrystallised material, $[\alpha]_D$ +79° (*c* 1·3). The acetate,[4,6,7] obtained by use of acetic anhydride–pyridine at 20° for 24 hr., was an oil, $[\alpha]_D$ +98° (*c* 1·1); the *methyl ether*, prepared by refluxing the alcohol with freshly prepared silver oxide in methyl iodide for 20 hr., had b. p. 140°/0·02 mm., $[\alpha]_D$ +85° (*c* 0·8) (Found: C, 83·95; H, 12·1. $C_{28}H_{48}O$ requires C, 83·9; H, 12·1%).

(*a*) The experiments, tabulated below, were carried out simultaneously with exclusion of moisture under identical conditions of temperature (20°) and humidity. 3 : 5-*cyclo*Cholestan-6α-ol (~200 mg.) in the appropriate solvent was treated with a 1% solution of bromine in the same solvent. In each case the usual isolation procedure gave an oil; each product was therefore chromatographed on aluminium oxide (10 g.) prepared in pentane. Repeated elution with pentane eluted cholesteryl bromide and 3β : 5 : 6β-tribromo-5α-cholestane; some columns were further eluted with more powerful eluants, but only small quantities of uncrystallisable oils were obtained.

A 1 : 1 synthetic mixture of cholesteryl bromide and 3β : 5 : 6β-tribromo-5α-cholestane (100 mg.) could not completely be separated on a long column of aluminium oxide (Spence,

XUM

Type H: 100 × wt. of sample). Elution with pentane gave a series of fractions: **No. 1, 83°, 25 mg.; 2, 83°, 35 mg.; 3, 85°, 10 mg.; 4, 88°, 10 mg.; 5, 91°, 8 mg.; 6, 95°, 5 mg.; 7, 95° 5 mg.; 8, 95°, 2 mg.** Determination of a few points on the temperature–composition diagram for mixtures of cholesteryl bromide, m. p. 98°, and 3β : 5 : 6β-tribromo-5α-cholestane, m. p. 111°, gave a simple two-branch curve with a eutectic at 79° corresponding to a content of 45% of cholesteryl bromide. From the diagram, the composition of the above eight chromatographic fractions was determined as 50, 50, 45, 39, 35, 25, 25, and 25% of cholesteryl bromide.

The following chromatographic details amplify the Table:

Bromination of 3 : 5-cyclo*cholestane*-6α-*ol.*

Exp. no.	Solvent	Alcohol (mg.)	Bromine (mol.)	Time (hr.)	Final soln.	Crude yield (mg.)	Al_2O_3 (Woelm)	Products * and yields
1	Ether	202	1	20	Colourless	251	Basic	Mono- (56%), tri-bromide (trace)
2	Ether	198	2·4	20	Colourless	331	Basic	Tribromide (63%)
3	Hexane	200	1·2	20	Colourless	325	Neutral	Mono- (69%), tri-bromide (trace)
4	Pentane	212	2·4	20	Colourless	321	Acid	Tribromide (69%)
5	Dioxan	203	2·4	24	Yellow	336	Acid	Mono- + tri-bromide
6	Chloroform	204	2·4	20	Yellow	338	Acid	Tribromide (60%)
7	Carbon tetrachloride	198	2·4	24	Orange	311	Neutral	Tribromide (50%)
8	*NN*-Dimethyl formamide	201	2·4	40	Yellow	—	Neutral	Tribromide (59%)
9	Acetic acid	200	2·4	24	Yellow	319	Basic	Tribromide (56%)
10	Chloroform	204	†	20 (in dark)	Orange	300	Acid	Mono- + tri-bromide

* Cholesteryl bromide and 3β : 5 : 6β-tribromo-5α-cholestane.
† Pyridinium sulphate dibromide.

Expt. 1. Fraction 1 (116 mg.), m. p. 98° (from acetone), undepressed by cholesteryl bromide, m. p. 96°; fraction 2 (14 mg.), m. p. 98—99° (from acetone), but some crystals had m. p. ~112°.

Expt. 2. Fraction 1 (195 mg.) [fraction 2 (2 mg.)], m. p. 112° (from ether–ethanol), undepressed by 3β : 5 : 6β-tribromo-5α-cholestane, m. p. 112°.

Expt. 3. Fractions 1 and 2 (160 mg.), m. p. 94—98° (from acetone), undepressed by authentic monobromide, m. p. 96°; some crystals from fraction 2 had m. p. ~112°, but little 3β : 5α : 6β-tribromide was present.

Expt. 4. Fraction 1 (199 mg.) and fraction 2 (15 mg.) [fraction 3 (1 mg.)], recrystallised from acetone, had m. p. 112°, undepressed by tribromide, m. p. 112°.

Expt. 5. Fractions 1 and 2 (142 mg.), fractions 3 and 4 (6 mg.), and fraction 5 (1 mg.) had m. p. <72° (from ether–ethanol). The united fractions were recrystallised from ether–ethanol; a portion did not dissolve easily, was separated, and found to be 3β : 5 : 6β-tribromo-5α-cholestane, m. p. and mixed m. p. 112°, whilst the soluble portion crystallised to give cholesteryl bromide, m. p. 89—94° (positive test with tetranitromethane in chloroform).

Expt. 6. Fractions 1, 2, and 3 (162 mg.), and fractions 4 and 5 (29 mg.) [fraction 6 (2 mg.)], all had m. p. ~110°, were united, and recrystallised from acetone, to give 3β : 5 : 6β-tribromo-5α-cholestane, m. p. and mixed m. p. 112°.

Expt. 7. Fractions 1 and 2 (156 mg.) [fractions 3 and 4 (1 mg.)] had m. p. ~110°, and from acetone–ethanol gave 3β : 5 : 6β-tribromo-5α-cholestane, m. p. and mixed m. p. 112—113°, $[\alpha]_D$ −51° (*c* 1·1).

Expt. 8. Fractions 1 and 2 (179 mg.) [fractions 3 and 4 (4 mg.)] had m. p. 108—110°, and from acetone–ethanol gave 3β : 5 : 6β-tribromo-5α-cholestane, m. p. and mixed m. p. 111—113°.

Expt. 9. Fraction 1 (173 mg.) [fraction 2 (3 mg.)] had m. p. 112—113° (from ethanol), undepressed by 3β : 5 : 6β-tribromo-5α-cholestane.

Expt. 10. Fractions 1 (155 mg.), 2 (17 mg.), and 3, 4, and 5 (together 10 mg.) were oily but crystallised from acetone to give material, m. p. 88—106°; this by recrystallisation from acetone gave impure cholesteryl bromide, m. p. 83—96° (positive test with tetranitromethane in chloroform); material from the mother-liquor, after five crystallisations from ether–ethanol, was impure 3β : 5α : 6β-tribromide, m. p. 105—111°.

3 : 5-*cyclo*Cholestan-6α-yl acetate (100 ± 4 mg.) in ether, pentane, chloroform, or carbon tetrachloride (20 c.c.) was treated with bromine (3·5 mol.) at 20° for 16—36 hr. The product, isolated in the usual way, in each case was an oil, which solidified when stirred with ethanol, and by recrystallisation gave the 3β : 5α : 6β-tribromide, m. p. and mixed m. p. 112°, in good yield. Similarly, the acetate (113 mg.) in acetic acid (25 c.c.) with a 2% solution of bromine in acetic acid (6 c.c., 3·5 mol.) at 20° for 30 hr., gave on dilution and filtration a solid (160 mg.),

which by recrystallisation from acetone–ethanol yielded the 3β : 5α : 6β-tribromide, m. p. and mixed m. p. 112—113°.

3 : 5-*cyclo*Cholestan-6α-yl methyl ether (100 mg.) in ether, pentane, chloroform, or carbon tetrachloride (20 c.c.) with bromine (3·7 mol.) at 20° for 16—30 hr. gave in each case a product, after the usual working up, which crystallised when stirred with ethanol and by recrystallisation from ethanol gave the 3β : 5α : 6β-tribromide, m. p. and mixed m. p. 112°.

One of us (R. W. R.) acknowledges the tenure of a University of Wales Postgraduate Studentship, and another (G. D. P.) the financial support of the Swansea Education Committee; we thank Glaxo Laboratories Ltd., Greenford, Middlesex, for a gift of cholesterol.

UNIVERSITY COLLEGE OF SWANSEA,
UNIVERSITY OF WALES.
DEPARTMENT OF ORGANIC CHEMISTRY, UNIVERSITY OF SYDNEY. [*Received, February 6th*, 1959.]

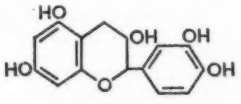
---

561. *Complex Formation between Copper and Some Organic Acids, Phenols, and Phenolic Acids occurring in Fruit.*

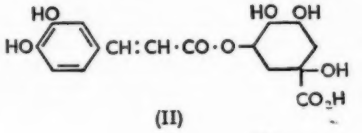
By C. F. TIMBERLAKE.

Cupric ions form complexes with (+)-catechin, chlorogenic acid, and caffeic acid.

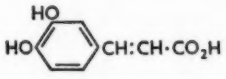
COMPLEX formation between cupric ions and catechol has been described.[1] Further potentiometric studies have shown that cupric ions can combine similarly with the *ortho*-diphenolic groups of (+)-catechin (I), chlorogenic acid (II),[2] and caffeic acid (III). In



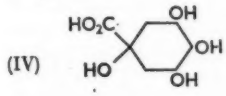
(I)



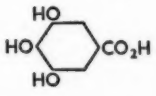
(II)



(III)



(IV)



(V)

acid solutions (pH <4) cupric ions combine with the carboxyl group of chlorogenic acid; the stabilities of the copper complexes of chlorogenic and quinic acids (IV) are compared with that of the dihydroshikimic acid (V) [3] complex.

Experimental.—Dilute solutions of the compounds (5 and 2·5 × 10^{-3}M) were titrated with alkali (5 × 10^{-2}N) at 25° with and without cupric chloride by the method previously described.[1] In the titrations without additions of potassium nitrate, pH was defined as equal to $-\log\{H^+\}$ where { } represents activity and ion-activity coefficients were evaluated from Davies's [4] equation. In the titrations with additions of potassium nitrate the volumes and concentrations of the solutions were such that ionic strengths were maintained relatively constant at 0·050—0·055; pH was then defined as equal to $-\log[H^+]$ where [ ] represents molar concentration.

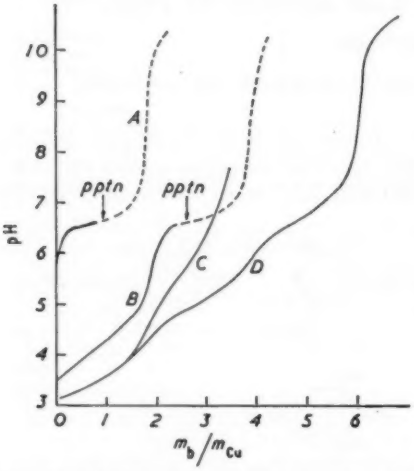
(+)-*Catechin complexes.* As with catechol, graphs relating the pH of solution to the ratio of concentration of added base to concentration of copper (m_b/m_{Cu}) obtained on titration of (+)-catechin solutions containing cupric chloride with sodium hydroxide showed inflections at (m_b/m_{Cu}) = 2 and 4, corresponding to the neutralisation of 2 and 4 hydrogen ions per atom of copper present. The values of pK_1 and pK_2 calculated from points on the buffer

[1] Timberlake, *J.*, 1957, 4987.
[2] Moores, McDermott, and Wood, *Analyt. Chem.*, 1948, **20**, 620.
[3] Carr, Pollard, Whiting, and Williams, *Biochem. J.*, 1957, **66**, 283.
[4] Davies, *J.*, 1938, 2093.

ranges were constant where, (+)-catechin being regarded as a tetrabasic acid H_4A, $K_1 = [CuH_2A]\{H^+\}^2/f_3[Cu^{2+}][H_4A]$ and $K_2 = f_2[Cu(H_2A)_2^{2-}]\{H^+\}^2/[CuH_2A][H_4A]$. The mean values found were $pK_1 = 7{\cdot}80$ ($I \longrightarrow 0$), $pK_2 = 11{\cdot}39$ ($I \longrightarrow 0$).

Dihydroshikimic acid complex. Potentiometric titrations of dihydroshikimic acid solutions with alkali showed a small liberation of hydrogen ions in the presence of cupric chloride. When the carboxyl group had been neutralised, further additions of alkali precipitated copper hydroxide (curve *B*, Figure). The dissociation constant of the carboxyl group of dihydroshikimic acid (HA) was $4{\cdot}1 \times 10^{-5}$ ($p_cK = 4{\cdot}39$) at zero ionic strength and $5{\cdot}1 \times 10^{-5}$ ($p_cK = 4{\cdot}29$) at $I = 0{\cdot}05$. The mean values of the stability constant of complex CuA^+ calculated from several pH values during early parts of the titrations were $K_s = [CuA^+]/f_3[Cu^{2+}][A^-]$; $\log K_s = 2{\cdot}08$ ($I \longrightarrow 0$) and $K_s = [CuA^+]/[Cu^{2+}][A^-]$; $\log K_s = 1{\cdot}65$ ($I = 0{\cdot}05$).

Quinic acid complexes. Potentiometric titrations of quinic acid solutions with alkali showed a small liberation of hydrogen ions in the presence of cupric chloride. On addition of alkali beyond that necessary to neutralise the carboxyl group, considerable liberation of hydrogen ions occurred, indicating appreciable complex formation (curve *C*). There was no precipitate and the solution became green. At pH values above 8, readings were unsteady.



Potentiometric titration.

A. Titration of 40 ml. of solution containing $CuCl_2,2H_2O$ (0·00125M) and KNO_3 (0·05M) with 0·05N-NaOH.
B. Titration of 40 ml. of solution containing dihydroshikimic acid (0·0025M), $CuCl_2,2H_2O$ (0·00125M), and KNO_3 (0·05M) with 0·05N-NaOH.
C. Titration of 40 ml. of solution containing quinic acid (0·0025M), $CuCl_2,2H_2O$ (0·00125M), and KNO_3 (0·05M) with 0·05N-NaOH.
D. Titration of 40 ml. of solution containing chlorogenic acid (0·0025M), $CuCl_2,2H_2O$ (0·00125M) and KNO_3 (0·05M) with 0·05N-NaOH.

The dissociation constant of the carboxyl group of quinic acid (HA) was $2{\cdot}6 \times 10^{-4}$ ($p_cK = 3{\cdot}58$) at zero ionic strength and $3{\cdot}2 \times 10^{-4}$ ($p_cK = 3{\cdot}50$) at $I = 0{\cdot}05$. The mean values of the stability constant of complex CuA^+ calculated from several pH values during the early parts of the titrations were $\log K_s = 2{\cdot}66$ ($I \longrightarrow 0$) and $\log K_s = 2{\cdot}44$ ($I = 0{\cdot}05$). The ncreased stability of CuA^+ of quinic acid (α-OH) over that of dihydroshikimic acid (α-H) is in accord with the findings of Lloyd, Wycherley, and Monk [5] for other monocarboxylic acids. The dissociation constant of quinic acid has been reported as $2{\cdot}2 \times 10^{-4}$ at 9°.[6]

Chlorogenic acid complexes. During the early part of the titration of chlorogenic acid solution containing cupric chloride with alkali, liberation of hydrogen ions was similar to that occurring with quinic acid. However on addition of nearly one equivalent of alkali (with respect to chlorogenic acid) the pH depression was greater than that which occurred with quinic acid (curve *D*). Further addition of alkali gave two well-defined buffer regions separated by inflections at intervals of $(m_b/m_{Cu}) = 2$. These findings suggest the formation of five-membered ring complexes between cupric ions and the *ortho*-diphenolic groups of chlorogenic acid.

Chlorogenic acid being regarded as H_3A, practically all the copper must be present as CuA^- at the inflection where $(m_b/m_{Cu}) = 4$. On further additions of alkali, CuA^- is converted into CuA_2^{4-} since constant values of K_2 were obtained from points on the buffer range $m_b/m_{Cu} = 4$—6, indicating that complexes CuA^- and CuA_2^{4-} were the only ones present.

[5] Lloyd, Wycherley, and Monk, *J.*, 1951, 1786.
[6] Heilbron, "Dictionary of Organic Compounds," Eyre and Spottiswoode, London, 1934.

The tabulated quantitative data were evaluated:

Dissociation constants of chlorogenic acid

	$I \longrightarrow 0$	$I = 0{\cdot}05$
Carboxyl group	${}_cK_1 = 2{\cdot}6 \times 10^{-4}$ ($p_cK_1 = 3{\cdot}59$)	${}_cK_1 = 3{\cdot}2 \times 10^{-4}$ ($p_cK_1 = 3{\cdot}50$)
First phenolic group	${}_cK_2 = 2{\cdot}6 \times 10^{-9}$ ($p_cK_2 = 8{\cdot}59$)	${}_cK_2 = 4{\cdot}5 \times 10^{-9}$ ($p_cK_2 = 8{\cdot}35$)

Gorter [7] has reported the dissociation constant (${}_cK_1$) of chlorogenic acid as $2{\cdot}2 \times 10^{-4}$ at 27°.

Stability constant of complex CuH_2A^+, *calculated from several* pH *readings during the early parts of the titrations.*

$K_s = [CuH_2A^+]/f_3[Cu^{2+}][H_2A^-]$; $\log K_s = 2{\cdot}72$ ($I \longrightarrow 0$)
$K_s = [CuH_2A^+]/[Cu^{2+}][H_2A^-]$; $\log K_s = 2{\cdot}42$ ($I = 0{\cdot}05$)

Equilibrium constant of the reaction $CuA^- + H_2A^- \rightleftharpoons CuA_2^{4-} + 2H^+$

$K_2 = f_4[CuA_2^{4-}][H^+]^2/f_1^2[CuA^-][H_2A^-]$; $pK_2 = 11{\cdot}4$ ($I \longrightarrow 0$)
$K_2 = [CuA_2^{4-}][H^+]^2/[CuA^-][H_2A^-]$; $pK_2 = 10{\cdot}3$ ($I = 0{\cdot}05$)

The activity equilibrium constant K_2 is probably subject to some error since it involves the activity coefficient of the quadrivalent ion CuA_2^{4-}.

The similarity of the stability constants of the copper complexes of quinic and chlorogenic acids indicates that at low pH values (<4) complex formation between cupric ions and the *ortho*-diphenolic groups of chlorogenic acid is very small.

The complexes existing with CuA^- in the buffer region at (m_b/m_{Cu}) = 2—4 have not yet been defined. In 1 : 1 mixtures of chlorogenic acid and cupric chloride ($2{\cdot}5 \times 10^{-3}$M), precipitation occurred midway along the buffer region in the vicinity of pH 5. The precipitated material contained 15·5% of copper. The calculated copper content of CuA^- or HACu, in which the carboxyl group is un-ionised, is 15·0%. The precipitate therefore may have been neutral HACu. If this were so, HACu should ionise according to equation $HACu \rightleftharpoons H^+ + CuA^-$ so that additions of base in this region neutralise the hydrogen ions liberated with formation of CuA^-. However, attempts to evaluate the experimental data by use of equations based on the presence of Cu^{2+}, CuH_2A^+, HACu, and CuA^- in various combinations did not give very consistent figures for the constants concerned, possibly owing to neglect of any complexes formed with the quinic acid part of the chlorogenic acid molecule in this pH region.

Support for the formation of HACu is obtained by consideration of Schwarzenbach's [8] work, who found that both copper and iron formed complexes containing an un-ionised sulphonic acid group with Tiron (catechol-3 : 5-disulphonic acid). The ionisation of the ferric complex $Fe[C_6H_2O_2SO_3[SO_3H)] \rightleftharpoons H^+ + Fe[C_6H_2O_2(SO_3)_2]^-$ occurs in acid solution.[9]

Caffeic acid complexes. Potentiometric titrations of solutions of caffeic acid (H_2A) and cupric chloride also indicated the formation of complexes CuA^- and CuA_2^{4-}. Consistent values of the stability constant of complex CuH_2A^+ were not obtained, probably owing to combination of cupric ions with the *ortho*-diphenolic groups of caffeic acid during the early stages of the titration, when the pH values were considerably higher than those found with chlorogenic acid. The tabulated quantitative data were evaluated.

Dissociation constants of caffeic acid

	$I \longrightarrow 0$	$I = 0{\cdot}05$
Carboxyl group	${}_cK_1 = 2{\cdot}4 \times 10^{-5}$ ($p_cK_1 = 4{\cdot}62$)	${}_cK_1 = 3{\cdot}2 \times 10^{-5}$ ($p_cK_1 = 4{\cdot}49$)
First phenolic group	${}_cK_2 = 8{\cdot}5 \times 10^{-10}$ ($p_cK_2 = 9{\cdot}07$)	${}_cK_2 = 1{\cdot}7 \times 10^{-9}$ ($p_cK_2 = 8{\cdot}76$)

The equilibrium constant of reaction $CuA^- + H_2A^- \longrightarrow CuA_2^{4-} + 2H^+$ is $pK_2 = 12{\cdot}1$ ($I \longrightarrow 0$); $pK_2 = 11{\cdot}0$ ($I = 0{\cdot}05$). The activity equilibrium constant is probably subject to some error since it involves the activity coefficient of the quadrivalent ion CuA_2^{4-}.

The natures of the ionic species in equilibrium with CuA^- during titration to the first

[7] Gorter, *Annalen*, 1911, **379**, 110.
[8] See Bjerrum, Schwarzenbach, and Sillén, "Stability Constants of Metal-Ion Complexes, with Solubility Products of Inorganic Substances. Part 1. Organic Ligands." Special Publication No. 6, The Chemical Society, London, 1957, Table 200.
[9] Willi and Schwarzenbach, *Helv. Chim. Acta*, 1951, **34**, 528.

XUM

inflection are still uncertain. Precipitation occurred at certain concentrations ($2{\cdot}5 \times 10^{-3}$M-caffeic acid and $1{\cdot}25 \times 10^{-3}$M-cupric chloride) suggesting that neutral CuHA containing a non-ionised carboxyl group may be formed.

It is considered that the solutions of chlorogenic acid and caffeic acid contained mainly the *trans*-isomers of these compounds.[10]

LONG ASHTON RESEARCH STATION,
BRISTOL UNIVERSITY.

[*Received, March 19th*, 1959.]

[10] Williams, *Chem. and Ind.*, 1955, 120.

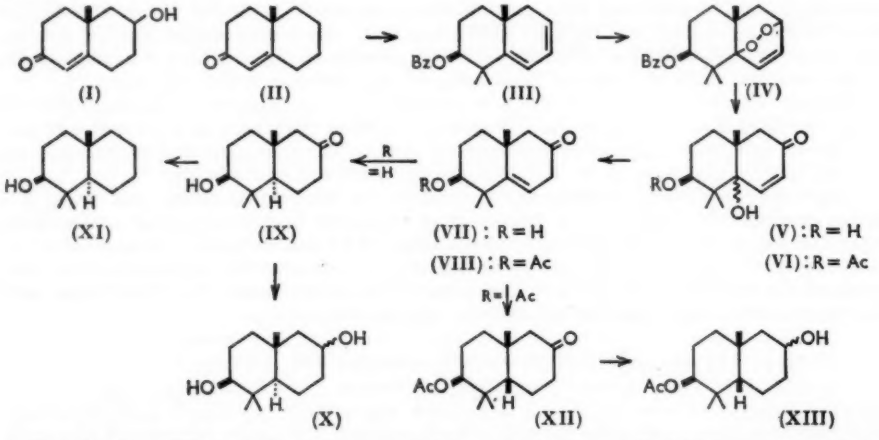
---

562. *Studies in the Synthesis of Terpenes. Part IV.* The Synthesis of* (±)-6β-*Hydroxy*-5 : 5 : 9β-*trimethyl*-trans-*decal*-2-*one*.

By T. G. HALSALL, W. J. RODEWALD, and (in part) D. WILLIS.

(±)-6β-Hydroxy-5 : 5 : 9β-trimethyl-*trans*-decal-2-one, a potential intermediate for the synthesis of higher terpenes, has been synthesised from 10-methyl-$\Delta^{1(9)}$-octal-2-one.

ONE of the potential intermediates for the synthesis of onocerin and of pentacyclic triterpenes of the β-amyrin type is the hydroxydecalone [1] (IX). A way of synthesising this appeared to be from derivatives of 4-hydroxy-2-methylcyclohexanone which, by analogy with 2-methylcyclohexanone, might be expected to condense with 4-diethylamino-butan-2-one to give the octalone (I). However, attempts to obtain this octalone from both the benzoate and the tetrahydropyranyl ether of 4-hydroxy-2-methylcyclohexanone were unsuccessful. The octalone has recently been prepared from the benzoate in about 2% yield by Sondheimer and Elad [2] but its further transformation to the decalone (IX) was not pursued.



The decalone (IX) has now been prepared in reasonable overall yield from the octalone (II).[3,4] This was converted into the diene (III) essentially by the method of King, Ritchie, and Timmons [5] (cf. the experimental section for brief details). The diene was then irradiated at room temperature in ethanol containing eosin (10% of the weight of diene) in

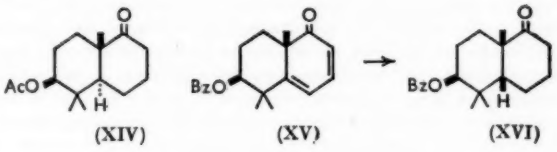
* Part III, *J.*, 1958, 624.

[1] Halsall and Thomas, *J.*, 1958, 2431.
[2] Sondheimer and Elad, *J. Amer. Chem. Soc.*, 1957, **79**, 5544.
[3] Du Feu, McQuillin, and Robinson, *J.*, 1937, 53.
[4] Gaspert, Halsall, and Willis, *J.*, 1958, 624.
[5] King, Ritchie, and Timmons, *Chem. and Ind.*, 1956, 1230.

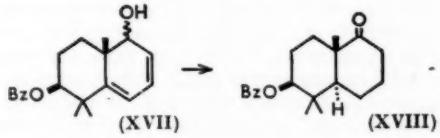
the presence of oxygen.[6] A product was obtained which at first appeared homogeneous but on crystallisation from ethanol gave two compounds as well as a small amount of oil. The main compound, obtained in 60% yield after recrystallisation, was the epidioxide (IV). Its structure, apart from the configuration of the epidioxide group, follows from the reactions subsequently carried out with it. The configuration is probably α, the 5- and 9-methyl groups preventing β-attack of oxygen. The other compound was isomeric with the epidioxide (IV).

When the epidioxide (IV) was treated with hot methanolic alkali, not only hydrolysis of the benzoate group but also rearrangement of the epidioxide group occurred. The product was the unsaturated ketone (V). In an attempt to cut down the losses involved in the crystallisation of the epidioxide (IV) the crude product from the irradiation was treated with alkali, it being expected that the resulting αβ-unsaturated ketone (V) would be readily separated from the simple hydrolysis product of the isomeric benzoate. The overall yield of ketone (V) obtained from the diene (III) by this procedure was much higher than that by the route involving crystallisation of the irradiation product. This suggested that the isomeric compound was produced after the irradiation and during the crystallisation of the epidioxide. This was proved by boiling the epidioxide in ethanol, the isomeric compound then being formed almost quantitatively. An analogous thermal rearrangement of an epidioxide is that of ascaridole to isoascaridole in hot xylene.[7] It is probable that the isomeric compound is analogous to isoascaridole. Its structure will be discussed in a later communication.

The alkaline rearrangement of the epidioxide (IV) to the ketone (V) is typical of secondary-tertiary epidoxides.[8,9] The light absorption of the ketone (V) ($\lambda_{max.}$ 2220 Å; ε 8950) and of its 6β-acetate (VI) shows the typical hypsochromic effect found with αβ-unsaturated γ-hydroxy-ketones.[8]



(XIV) (XV) (XVI)



(XVII) (XVIII)

The γ-hydroxy-ketone (V) was reduced with zinc dust in boiling acetic acid[10] to the βγ-unsaturated ketone (VII); no evidence was found for the presence of the conjugated ketone. Hydrogenation of the ketone (VII) with palladium–charcoal in ethanol or acetic acid gave the *trans*-decalone (IX). Hydrogention with Adams platinum catalyst in acetic acid afforded the *trans*-decalindiol (X) which was similarily obtained from the *trans*-decalone. No *cis*-decalin derivative was found in the products of these hydrogenations.

Wolff–Kishner reduction of the *trans*-decalone gave the known *trans*-decalol (XI).[4]

[6] Cf. Bergmann and McLean, *Chem. Rev.*, 1941, **28**, 367; Bladon, Clayton, Greenhalgh, Henbest, Jones, Lovell, Silverstone, Wood, and Woods, *J.*, 1952, 4883; Clayton, Henbest, and Jones, *J.*, 1953, 2015; Bladon, *J.*, 1955, 2176.

[7] Henry and Paget, *J.*, 1921, **119**, 1722; Simonsen, "The Terpenes," Cambridge Univ. Press, 2nd edn., Vol. I, p. 447.

[8] Cf. Conca and Bergmann, *J. Org. Chem.*, 1953, **18**, 1104.

[9] Cf. Laubach, Schreiber, Agnello, Lightfoot, and Brunings, *J. Amer. Chem. Soc.*, 1953, **75**, 1514; Kornblum and de la Mare, *ibid.*, 1951, **73**, 880.

[10] Cf. Rosenfeld and Gallagher, *ibid.*, 1955, **77**, 4367, and references cited therein.

XUM

This has also been obtained from the acetoxydecalone [4] (XIV) which has been shown by Sondheimer and Elad [11] to have the acetoxyl and the angular methyl group *cis*-related.

Acetylation of the unsaturated γ-hydroxy-ketone (V) gave the 6β-monoacetate (VI). Reduction of this with zinc dust in acetic acid gave the β-unsaturated acetoxy-ketone (VIII). Hydrogenation with palladium–charcoal then gave the acetoxydecalone (XII). This must be a *cis*-decalin derivative as it and the alcohol derived from it are different from the corresponding *trans*-decalone (IX) and its acetate. Hydrogenation with Adams platinum catalyst gave the acetoxy-*cis*-decalol (XIII), also obtained by hydrogenation of the corresponding ketone (XII). The unpredictability of the course of hydrogenation is further illustrated by the results of Haynes and Timmons [12] who have shown that hydrogenation of the dienone (XV) gives a *cis*-decalone (XVI), whilst hydrogenation of the dienol (XVII) followed by oxidation of the resulting alcohol afforded the *trans*-decalone (XVIII).

Experimental

M. p.s were determined on a Kofler block and are corrected. The light petroleum used for chromatography had b. p. 40—60°; that used for crystallisations had b. p. 60—80°. The alumina used for chromatography was " Peter Spence, Grade H," deactivated with 5% of 10% acetic acid.

(±)-2β-*Benzoyloxy*-1 : 2 : 3 : 4 : 5 : 10-*hexahydro*-1 : 1 : 10β-*trimethylnaphthalene*.—This was prepared by the following reactions essentially according to the method of Haynes, King, Ritchie, and Timmons.[5,13] 10-Methyl-$\Delta^{1(9)}$-octal-2-one was prepared from 2-methylcyclohexanone and 4-diethylaminobutan-2-one. It was methylated with methyl iodide in the presence of sodium t-amyloxide, to give 1 : 1 : 10-trimethyl-Δ^{9}-octal-2-one in 80% yield. This in turn was converted into 2β-benzoyloxy-1 : 1 : 10β-trimethyl-Δ^{9}-octalin, m. p. 87—89° (Haynes, King, Ritchie, and Timmons [13] give m. p. 87—89°), in 40—50% yield by reduction with sodium in boiling ethanol and benzoylation of the crude product.

The benzoate, with *N*-bromosuccinimide in boiling carbon tetrachloride, gave the 7-bromo-derivative, m. p. 153—155° (Haynes, King, Ritchie, and Timmons [13] give m. p. 153—155°), in 95% yield. This was dehydrobrominated by heating it in ethanol, (±)-2β-benzoyloxy-1 : 2 : 3 : 4 : 5 : 10-hexahydro-1 : 1 : 10β-trimethylnaphthalene, m. p. 103—105° (Haynes, King, Ritchie, and Timmons [13] give m. p. 101—104°), being obtained in 90% yield.

The last benzoate with aqueous-alcoholic potassium hydroxide gave (±)-2β-*hydroxy*-1 : 2 : 3 : 4 : 5 : 10-*hexahydro*-1 : 1 : 10β-*trimethylnaphthalene* as prisms (from light petroleum), m. p. 83—84° (Found: C, 80·9; H, 10·8. $C_{13}H_{20}O$ requires C, 81·2; H, 10·5%), $\lambda_{max.}$ 2650 Å (ε 3700). The hydroxy-compound (2·52 g.), with acetic anhydride (3 c.c.) and pyridine (10 c.c.) in the usual way, afforded an oil which was taken up in light petroleum and filtered through alumina (10 g.) along with light petroleum (100 c.c.). Evaporation of the solvent and distillation of the product gave (±)-2β-*acetoxy*-1 : 2 : 3 : 4 : 5 : 10-*hexahydro*-1 : 1 : 10β-*trimethylnaphthalene* (2·27 g.), b. p. 62°/0·03 mm., $n_D^{12·5}$ 1·5065 (Found: C, 77·0; H, 9·75. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·45), $\nu_{max.}$ 1740 (OAc), 1680 and 700 cm.$^{-1}$ (no band due to OH), $\lambda_{max.}$ 2640 Å (ε 3940).

(±)-2β-*Benzoyloxy*-6 : 9-*epidioxy*-1 : 1 : 10β-*trimethyl*-Δ^{7}-*octalin* (IV).—Dry oxygen was passed into (±)-2β-benzoyloxy-1 : 2 : 3 : 4 : 5 : 10-hexahydro-1 : 1 : 10β-trimethylnaphthalene (10 g.) in ethanol (300 c.c.) containing eosin (1·0 g.) and illuminated by a 500-watt lamp placed beneath the reaction flask which was kept at 17° by immersion in flowing water. After 6 hr. a solid began to separate. After 24 hr. irradiation was stopped, and the mixture kept at 0° overnight. The resulting solid (A) (7·0 g.), m. p. 162°, was removed. Evaporation of the solvent at a low temperature afforded a further quantity of solid (B) (3·15 g.), m. p. ~160°, and an oil (C) (1·0 g.). The solid (B) was extracted with benzene to separate it from eosin. The resulting benzene solution was evaporated, and the residue combined with solid (A) and crystallised several times from ethanol, to give two compounds: (i) (±)-2β-*benzoyloxy*-6 : 9-*epidioxy*-1 : 1 : 10β-*trimethyl*-Δ^{7}-*octalin* (6·6 g., 60%), elongated prisms, m. p. 168° (softening at 160°) (Found: C, 73·05; H, 7·5. $C_{20}H_{24}O_4$ requires C, 73·15; H, 7·35%), $\nu_{max.}$ 1728 (benzoate), 1380 and 1368 (*gem*-dimethyl)

[11] Sondheimer and Elad, *J. Amer. Chem. Soc.*, 1958, **80**, 1967.
[12] Haynes and Timmons, *Proc. Chem. Soc.*, 1958, 345.
[13] Haynes, King, Ritchie, and Timmons, unpublished work.

and 888 cm.$^{-1}$ (epidioxide), and (ii) an isomeric *benzoate* (3·4 g., 31%), plates, m. p. 172° (softening at 165°) (Found: C, 72·85; H, 7·15. $C_{30}H_{24}O_4$ requires C, 73·15; H, 7·35%), $\nu_{max.}$ 1728 (benzoate), 1378 and 1362 (*gem*-dimethyl), and 910 and 828 cm.$^{-1}$ (epoxy-groups?).

(±)-6β : 10ξ-*Dihydroxy*-5 : 5 : 9β-*trimethyl*-Δ^3-*octal*-2-*one* (V).—(*a*) The epidioxide benzoate (IV) (1·0 g.) was heated under reflux in aqueous-methanolic potassium hydroxide (10%; 25 c.c.) for 1 hr. After removal of the methanol under reduced pressure, dilution with water and extraction with chloroform afforded (±)-6β : 10ξ-*dihydroxy*-5 : 5 : 9β-*trimethyl*-Δ^3-*octal*-2-*one* which crystallised from ethanol–light petroleum (1 : 25) as prisms (670 mg., 98%), m. p. 181° (Found: C, 69·65; H, 9·25. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%), $\lambda_{max.}$ 2220 Å (ε 8800), $\nu_{max.}$ 3460 (OH), 1680 (C=C–C=O), 1382 and 1368 cm.$^{-1}$ (*gem*-dimethyl). The *semicarbazone* was obtained as plates (from aqueous ethanol), m. p. 254—255° (decomp.) (Found: C, 59·95; H, 8·3; N, 15·15. $C_{14}H_{23}O_3N_3$ requires C, 59·75; H, 8·25; N, 14·95%).

(*b*) (±)-2β-Benzoyloxy-1 : 2 : 3 : 4 : 5 : 10-hexahydro-1 : 1 : 10β-trimethylnaphthalene (15 g.) was irradiated in ethanol (350 c.c.) containing eosin (1·5 g.) in the presence of oxygen as above. After 6 hr. a solid began to separate. After irradiation for 28 hr. the mixture was kept at 0° overnight; a solid (12·5 g., m. p. 162—165°) separated. It was isolated and washed with ethanol. Low-temperature evaporation of the solvent afforded a further quantity of solid (2 g.; m. p. 160—163°) and an oil (~2·0 g.).

The solids were combined and part (500 mg.) was adsorbed from benzene (15 c.c.) on alumina (30 g.). Elution with benzene–light petroleum (1 : 1) afforded (±)-2β-benzoyloxy-6 : 9-epidioxy-1 : 1 : 10β-trimethyl-Δ^7-octalin (490 mg.) as prisms, m. p. 168° [after one recrystallisation from benzene–light petroleum (2 : 1)].

The combined solids (10 g.) were heated under reflux with aqueous-methanolic potassium hydroxide (10%; 200 c.c.) for 3 hr. After removal of the solvent under reduced pressure and dilution with water, extraction with chloroform afforded (±)-6β : 10ξ-dihydroxy-5 : 5 : 9β-trimethyl-Δ^3-octal-2-one as needles (6·30 g.) [from ethanol–light petroleum (1 : 25)], m. p. 181°.

Rearrangement of (±)-2β-*Benzoyloxy*-6 : 9-*epidioxy*-1 : 1 : 10β-*trimethyl*-Δ^7-*octalin in Boiling Ethanol*.—The epidioxide benzoate (500 mg.) was heated under reflux in ethanol (50 ml.) for 5 hr. The solution was then concentrated and the product, m. p. 169—170°, was recrystallised twice from ethanol to give the isomeric benzoate described above as plates (450 mg.), m. p. 172°.

(±)-6β-*Hydroxy*-5 : 5 : 9β-*trimethyl*-Δ^4-*octal*-2-*one* (VII).—6β : 10-Dihydroxy-5 : 5 : 9β-trimethyl-Δ^3-octal-2-one (1·8 g.) in boiling acetic acid (40 c.c.) was treated during 15 min. with small portions of zinc dust (2·2 g.). The mixture was heated under reflux for a further 5 min. and then filtered, the residue being washed with chloroform. After addition of further chloroform to the filtrate, the acetic acid was removed by washing with aqueous sodium hydrogen carbonate. A viscous oil was isolated from the chloroform solution. It was adsorbed from benzene–light petroleum (1 : 3) on deactivated alumina (150 mg.). Elution with the same solvent mixture gave (±)-6β-*hydroxy*-5 : 5 : 9β-*trimethyl*-Δ^4-*octal*-2-*one* which crystallised from ether–light petroleum (1 : 6) as prisms (1·2 g., 72%), m. p. 99° (Found: C, 74·8; H, 9·75. $C_{13}H_{20}O_2$ requires C, 74·95; H, 9·7%), $\lambda_{max.}$ 2800 Å (ε 39), $\nu_{max.}$ 3450 (OH), 1715 (sat. C=O), 1375 and 1360 (*gem*-dimethyl), 812 and 793 cm.$^{-1}$ (trisubstituted double bond). The octalone was not very stable. If it was kept dissolved in ethanol, ether, acetone, or light petroleum for some time, much oil was obtained on evaporation. The dry crystals began to soften after several weeks.

Elution with ether gave a light yellow oil (300 mg.), which crystallised from ether to give prisms (30 mg.), m. p. 264°. From the mother-liquor a further solid (20 mg.) was obtained after recrystallisation from ethanol–light petroleum. Further crystallisation from ethanol gave yellow prisms, m. p. 228—230°.

Hydrogenation of (±)-6β-*Hydroxy*-5 : 5 : 9β-*trimethyl*-Δ^4-*octal*-2-*one* (VII).—(*a*) The octalone (400 mg.) was hydrogenated in ethanol (40 c.c.) with previously hydrogenated 10% palladium–charcoal (400 mg.). Hydrogenation was stopped after 50 min. when 1·03 mol. had been taken up. Removal of the catalyst and evaporation of the solvent gave (±)-6β-*hydroxy*-5 : 5 : 9β-*trimethyl*-trans-*decal*-2-*one* (IX) as prisms (380 mg., 94%) (from ether), m. p. 144—145° (sublimation at 115°) (Found: C, 74·0; H, 10·6. $C_{13}H_{22}O_2$ requires C, 74·25; H, 10·55%), $\nu_{max.}$ (in "Nujol") 3450 (OH), 1700 (C=O), 1382 and 1360 cm.$^{-1}$ (*gem*-dimethyl) (no band at 812 or 793 cm.$^{-1}$).

(*b*) The octalone (200 mg.) was hydrogenated in acetic acid (30 c.c.) with previously hydrogenated 10% palladium–charcoal (200 mg.). After 75 min. 1·0 mol. had been absorbed

and hydrogenation was stopped. After removal of the catalyst and solvent, crystallisation from ether gave (±)-6β-hydroxy-5 : 5 : 9β-trimethyl-*trans*-decal-2-one (165 mg.), m. p. and mixed m. p. 144—145°.

(*c*) An attempt to hydrogenate the octalone (200 mg.) in ethyl acetate (20 c.c.) with Adams platinum catalyst (100 mg.) failed. Acetic acid (2 c.c.) was added and a slow uptake of hydrogen then took place. The reaction was stopped after 1 mol. had been absorbed. Removal of the catalyst and solvent gave a viscous oil, which was dissolved in ether and treated with light petroleum. The resultant precipitate (130 mg.) was crystallised several times from ether–light petroleum (1 : 10), to give 6β-hydroxy-5 : 5 : 9β-trimethyl-*trans*-decal-2-one (80 mg.), m. p. 144—145°, and 2ξ : 6β-dihydroxy-5 : 5 : 9β-trimethyl-*trans*-decalin (see next paragraph) (50 mg.), m. p. 190°.

(*d*) The octalone (200 mg.) in acetic acid (20 c.c.) was hydrogenated with Adams platinum catalyst (50 mg.). Uptake (2·05 mol.) ceased after 45 min. Removal of the catalyst and solvent afforded a solid which, crystallised from ether–light petroleum (1 : 5), gave 2ξ : 6β-*dihydroxy*-5 : 5 : 9β-*trimethyl*-trans-*decalin* (X) as prisms (180 mg.), m. p. 190° (Found: C, 73·4; H, 11·25. $C_{15}H_{24}O_2$ requires C, 73·55; H, 11·4%), $\nu_{max.}$ (in " Nujol ") 3350 cm.$^{-1}$ (OH) (no band indicative of C=O or trisubstituted double bond).

(*e*) The octalone (200 mg.) in ethanol (15 c.c.) was hydrogenated with Adams platinum catalyst (50 mg.). Absorption of hydrogen (0·8 mol.) was very slow and ceased after 4 hr. Removal of the catalyst and solvent gave a viscous oil which was adsorbed on deactivated alumina (20 g.). Elution with light petroleum–benzene (1 : 4) afforded starting material (120 mg., 60%). Elution with benzene gave an oil (35 mg.) which was not investigated further. Elution with ether yielded a solid (40 mg.) which crystallised from ether–light petroleum (1 : 3) to give 2ξ : 6β-dihydroxy-5 : 5 : 9β-trimethyl-*trans*-decalin (20 mg.), m. p. 190°, and a compound (15 mg.) (prisms), m. p. 211° (partial sublimation 205°) (Found: C, 68·35; H, 10·5%), $\nu_{max.}$ (in " Nujol ") at 3300 (OH) and 812 cm.$^{-1}$ (double bond) (no C=O band).

Hydrogenation of 6β-*Hydroxy*-5 : 5 : 9β-*trimethyl*-trans-*decal*-2-*one*.—The decalone (200 mg.) in acetic acid (20 c.c.) was hydrogenated with Adams platinum catalyst (50 mg.). Reaction was stopped after 20 min. when 1 mol. had been absorbed. Removal of the catalyst and solvent gave 2ξ : 6β-dihydroxy-5 : 5 : 9β-trimethyl-*trans*-decalin (195 mg.) (prisms from ether–light petroleum), m. p. and mixed m. p. 190°.

6β-*Acetoxy*-5 : 5 : 9β-*trimethyl*-trans-*decal*-2-*one*.—6β-Hydroxy-5 : 5 : 9β-trimethyl-*trans*-decal-2-one (60 mg.) in pyridine (1·5 c.c.) with acetic anhydride (0·15 c.c.) at 100° for 30 min. gave a product which crystallised from ether–light petroleum (1 : 6) to give 6β-*acetoxy*-5 : 5 : 9β-*trimethyl*-trans-*decal*-2-*one* as prisms (~70 mg.), m. p. 113°, depressed to 105—110° on admixture with the corresponding *cis*-decalone (see below) (Found: C, 71·45; H, 9·25. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·6%).

Wolff–Kishner Reduction of (±)-6β-*Hydroxy*-5 : 5 : 9β-*trimethyl*-trans-*decal*-2-*one* (IX).—The hydroxydecalone (700 mg.) in redistilled diethylene glycol (15 c.c.) was heated under reflux for 1 hr. under nitrogen with 100% hydrazine hydrate (1·4 c.c.) and potassium hydroxide (1·3 g.). The excess of water was then removed by distillation until the internal temperature reached 180°. Heating under reflux was then continued for a further 3 hr. under nitrogen. After dilution with water, ether-extraction afforded a solid (380 mg.) which on sublimation at 110—115°/12 mm. gave (±)-1 : 1 : 10β-trimethyl-*trans*-decalin-2β-ol (XI) as plates, m. p. and mixed m. p. 60—65° (Found: C, 79·85; H, 12·05. Calc. for $C_{13}H_{24}O$: C, 79·5; H, 12·3%), $\nu_{max.}$ (in " Nujol ") 3300 (OH) (no C=O band). The infrared spectrum was identical with that of authentic (±)-1 : 1 : 10β-trimethyl-*trans*-decalin-2β-ol.[4]

(±)-6β-*Acetoxy*-10ξ-*hydroxy*-5 : 5 : 9β-*trimethyl*-Δ^3-*octal*-2-*one* (VI).—6β : 10ξ-Dihydroxy-5 : 5 : 9β-trimethyl-Δ^3-octal-2-one (790 mg.) in pyridine (5 c.c.) with acetic anhydride (0·4 c.c.) at 100° for 1 hr. gave a product, m. p. 105—108°. Crystallisation from ethanol–light petroleum (1 : 20) gave (±)-6β-*acetoxy*-10ξ-*hydroxy*-5 : 5 : 9β-*trimethyl*-Δ^3-*octal*-2-*one* as plates (910 mg., 97%), m. p. 110°, resolidifying partially as prisms, m. p. 127° (Found: C, 67·3; H, 8·2. $C_{15}H_{22}O_4$ requires C, 67·65; H, 8·35%), $\lambda_{max.}$ 2220 Å (ε 8950), $\nu_{max.}$ 3620 and 3500 (OH), 1740 and 1240 (OAc), 1685 cm.$^{-1}$ (C=C–C=O).

Zinc Reduction of (±)-6β-*Acetoxy*-10ξ-*hydroxy*-5 : 5 : 9β-*trimethyl*-Δ^3-*octal*-2-*one*.—Zinc dust (1·8 g.) was added in small portions during 15 min. to a boiling solution of the octalone (1·7 g.) in acetic acid. The hot solution was filtered, the residue being washed with chloroform. The product was isolated as a viscous oil with chloroform, acetic acid being removed by washing

with aqueous sodium hydrogen carbonate solution. The oil was absorbed from benzene (15 c.c.) on deactivated alumina (150 g.). Elution with light petroleum–benzene (2 : 3) (800 c.c.) gave (±)-6β-*acetoxy*-5 : 5 : 9β-*trimethyl*-$\Delta^{4(10)}$-*octal*-2-*one* (VIII) (1·2 g., 75%), m. p. 64—66°, which crystallised from ether as plates, m. p. 67° (Found: C, 72·05; H, 8·8. $C_{15}H_{22}O_3$ requires C, 71·95; H, 8·85%), $\lambda_{max.}$ 2850 Å (ε 38), ε_{2100} 1100, ε_{2150} 715, ε_{2200} 540, $\nu_{max.}$ 1738 and 1238 (OAc), shoulders at 1722 and 1708 cm.$^{-1}$, $\nu_{max.}$ (in " Nujol ") 1695 cm.$^{-1}$ (C=O).

The acetoxyoctalone is not very stable. After several hours' in solution in organic solvents a viscous oil (polymer?) results. The crystals soften after several weeks.

Elution with light petroleum–benzene (2 : 3) (600 c.c.) gave a liquid fraction (100 mg.); addition of ether afforded a solid which crystallised from ethanol as light yellow prisms (substance A) (40 mg.), m. p. 266—267°, partial sublimation at 230° (Found: C, 73·1; H, 8·7%), $\lambda_{max.}$ (in chloroform) 2500 and 3550 Å ($E^{1\%}_{1\,cm.}$ 304, 410), $\nu_{max.}$ (in " Nujol ") 1732 and 1240 (OAc), 1695 (C=O), 1610 and 1580 cm.$^{-1}$ (no OH band).

Further elution with benzene (600 c.c.) and ether (400 c.c.) gave two liquid fractions (80 and 150 mg.). Several crystallisations of both fractions from alcohol or alcohol–light petroleum (1 : 4) afforded light yellow needles (*substance B*) (~100 mg.), m. p. 212—214°, resolidifying partially as yellow prisms, m. p. 253—254° (Found: C, 71·8; H, 7·75%; *M*, 408), $\lambda_{max.}$ (in chloroform) 2550 and 3550 Å ($E^{1\%}_{1\,cm.}$ 290, 457), $\nu_{max.}$ (in " Nujol ") 1730 and 1247 (OAc), 1710, 1685, 1590, 1575, 810, and 865 cm.$^{-1}$.

Substances A and B are probably acetates of the corresponding compounds, m. p. 264° and 228—230°, obtained as by-products from the reduction of 6β : 10ξ-dihydroxy-5 : 5 : 9β-trimethyl-Δ^3-octal-2-one with zinc.

Hydrogenation of (±)-6β-*Acetoxy*-5 : 5 : 9β-*trimethyl*-$\Delta^{4(10)}$-*octal*-2-*one*.—(*a*) The octalone (400 mg.) was hydrogenated in ethanol (40 c.c.) with previously hydrogenated 10% palladium–charcoal (400 mg.). After 30 min. 1·05 mol. had been absorbed and reaction was stopped. Removal of the catalyst and solvent gave a liquid which was dissolved in ether. Addition of light petroleum (4 vols.) gave (±)-6β-*acetoxy*-5 : 5 : 9β-*trimethyl*-cis-*decal*-2-*one* (XII) as prisms (220 mg., 54%), m. p. 108°, raised by further crystallisation from ether–light petroleum to 111°, depressed to 105—110° on admixture with the corresponding *trans*-decalone, m. p. 113° (Found: C, 71·3; H, 9·5. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·6%), $\nu_{max.}$ 1735 and 1240 (OAc), shoulder at 1725 cm.$^{-1}$ (C=O) (no band indicative of trisubstituted double bond). The spectrum was similar to that of (±)-6β-acetoxy-5 : 5 : 9β-trimethyl-*trans*-decal-2-one but differences were found at 1325, 1144, and 777 cm.$^{-1}$.

The acetate (100 mg.) was hydrolysed under reflux for 30 min. in 10% aqueous-methanolic potassium hydroxide (5 c.c.). The resulting (±)-6β-*hydroxy*-5 : 5 : 9β-*trimethyl*-cis-*decal*-2-*one* crystallised from ether–light petroleum as prisms (75 mg.), m. p. 111°, depressed to 106—111° on admixture with (±)-6β-hydroxy-5 : 5 : 9β-trimethyl-*trans*-decal-2-one (m. p. 144—145°) (Found: C, 74·35; H, 10·2. $C_{13}H_{22}O_2$ requires C, 74·25; H, 10·55%), $\nu_{max.}$ (in " Nujol ") 3400 (OH), 1702 cm.$^{-1}$ (C=O) (no band due to OAc). The spectrum was very similar to that of 6β-hydroxy-5 : 5 : 9β-trimethyl-*trans*-decal-2-one, but there was a small difference at 1133 cm.$^{-1}$.

(*b*) The octalone (200 mg.) was hydrogenated in acetic acid (15 c.c.) with Adams platinum catalyst (100 mg.). Uptake ceased after 85 min. (2 mol.). Removal of the catalyst and solvent afforded (±)-6β-*acetoxy*-5 : 5 : 9β-*trimethyl*-cis-*decalin*-2ξ-*ol* which crystallised from ether–light petroleum (1 : 4) as prisms (90 mg., 44%), m. p. 124° (Found: C, 71·0; H, 10·5. $C_{15}H_{24}O_3$ requires C, 70·8; H, 10·3%), $\nu_{max.}$ 3610 (OH), 1736 and 1240 cm.$^{-1}$ (OAc) (no band for C=O or trisubstituted double bond).

The acetate (50 mg.) was hydrolysed under reflux for 20 min. in 10% aqueous-methanolic potassium hydroxide (4 c.c.). The resulting (±)-5 : 5 : 9β-*trimethyl*-cis-*decalin*-2ξ : 6β-*diol* crystallised from ethanol–light petroleum as prisms (40 mg.), m. p. 158° (Found: C, 73·45; H, 11·4. $C_{13}H_{24}O_2$ requires C, 73·55; H, 11·4%), $\nu_{max.}$ (in " Nujol ") 3450 cm.$^{-1}$ (OH) (no band for OAc, C=O, or trisubstituted double bond).

Hydrogenation of (±)-6β-*Acetoxy*-5 : 5 : 9β-*trimethyl*-cis-*decal*-2-*one*.—The acetoxy-decalone (200 mg.) was hydrogenated in acetic acid (15 c.c.) in the presence of Adams platinum catalyst (50 mg.). The hydrogenation (1 mol.) was stopped after 1·5 hr. Removal of the catalyst and solvent gave an oil which gave crystals, m. p. 110—120°, from ether (0·5 ml.). The crystals were recrystallised from ether–light petroleum (1 : 4) to give (±)-6β-acetoxy-5 : 5 : 9β-trimethyl-*cis*-decalin-2ξ-ol as prisms (25 mg.), m. p. and mixed m. p. 124°.

Hydrogenation of (±)-6β : 10ξ-*Dihydroxy*-5 : 5 : 9β-*trimethyl*-Δ^3-*octal*-2-*one*.—The octalone

(500 mg.) in ethanol (30 c.c.) was hydrogenated with Adams platinum catalyst (80 mg.); 1·03 mol. was absorbed in 20 min. after which hydrogenation was stopped. Removal of the catalyst and solvent gave crude (±)-6β : 10ξ-*dihydroxy*-5 : 5 : 9β-*trimethyldecal*-2-*one* (500 mg.), m. p. 165°. Several crystallisations from ethanol–light petroleum (b. p. 60—80°) (1 : 20) afforded two types of crystal: needles, m. p. 170° (Found: C, 68·95; H, 9·9. $C_{13}H_{22}O_3$ requires C, 69·0; H, 9·6%), and prisms, m. p. 199° (Found: C, 69·0; H, 9·6%). These two forms were polymorphs since slow crystallisation of the former from ethanol–light petroleum (b. p. 60—80°) (1 : 5) gave the latter, and quick recrystallisation of the latter from light petroleum (b. p. 60—80°)–ether (20 : 1) afforded the former. Both forms had $\lambda_{max.}$ 2850 Å (ε 16), $\nu_{max.}$ (in "Nujol") 3410 (OH) and 1695 (sat. C=O) (no band due to –C=C–C=O or double bond). They gave the same *acetate*: *e.g.*, the form, m. p. 170° (350 mg.), in pyridine (3 c.c.) with acetic anhydride (0·2 c.c.) at 100° for 30 min. gave prisms [from light petroleum (b. p. 60—80°)–ethanol (10 : 1)], m. p. 138° (Found: C, 67·3; H, 9·15. $C_{15}H_{24}O_4$ requires C, 67·15; H, 9·0%).

The authors thank Dr. Timmons for details of the preparation of the diene (III) and Professor E. R. H. Jones, F.R.S., for his interest. One of them (W. J. R.) thanks the Polish Ministry of Science and the British Council for scholarships and another (D. W.) the C.S.I.R.O., Australia, for a maintenance grant.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, March 6th,* 1959.]

---

563. *Solutions in Sulphuric Acid. Part XXV.* Cryoscopic Measurements on Some Phenols.*

By R. J. GILLESPIE and J. V. OUBRIDGE.

It is concluded from cryoscopic measurements that when dissolved in sulphuric acid at room temperature phenol and *p*-cresol are rapidly sulphonated and esterified, *o*- and *m*-nitrophenol are rapidly esterified but not sulphonated, *p*-nitrophenol is partly esterified and partly sulphonated, and 2 : 4-dinitrophenol is partially protonated.

CRYOSCOPIC and conductometric measurements have shown that methyl and ethyl alcohols give stable solutions of methyl and ethyl hydrogen sulphates respectively when dissolved in sulphuric acid:

$$ROH + 2H_2SO_4 = RHSO_4 + H_3O^+ + HSO_4^-$$

Many other alcohols show a similar initial behaviour but the solutions of their hydrogen sulphates are not stable; oxidation and other reactions occur.[1] Some aryl-substituted alcohols give the corresponding carbonium ion, *e.g.*,

$$Ph_3C{\cdot}OH + 2H_2SO_4 = Ph_3C^+ + H_3O^+ + 2HSO_4^-$$

With the exception of picric acid, which cryoscopy has shown to be a non-electrolyte,[2] no previous cryoscopic or conductometric measurements have been made on solutions of phenols in sulphuric acid. The most probable of the possible modes of ionisation or reaction that phenols might undergo in sulphuric acid and the corresponding values of ν,

* Part XXIV, *J.*, 1958, 667.

[1] See, *e.g.*, Gillespie and Leisten, *Quart. Rev.*, 1954, **8**, 40.
[2] Brayford and Wyatt, *J.*, 1955, 3453; Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1933, **55**, 1900.

XUM

the total number of moles of ions and molecules produced by one mole of the phenol, would appear to be the following:

(1) Protonation

$$C_6H_5{\cdot}OH + H_2SO_4 = C_6H_5{\cdot}OH_2^+ + HSO_4^- \quad \nu = 2$$

(2) Esterification

$$C_6H_5{\cdot}OH + 2H_2SO_4 = C_6H_5{\cdot}HSO_4 + HSO_4^- + H_3O^+ \quad \nu = 3$$

(3) (*a*) Mono-sulphonation

$$C_6H_5{\cdot}OH + 2H_2SO_4 = HSO_3{\cdot}C_6H_4{\cdot}OH + HSO_4^- + H_3O^+ \quad \nu = 3$$

(*b*) Di-sulphonation

$$C_6H_5{\cdot}OH + 4H_2SO_4 = (HSO_3)_2C_6H_3{\cdot}OH + 2HSO_4^- + 2H_3O^+ \quad \nu = 5$$

(4) Carbonium-ion formation

$$C_6H_5{\cdot}OH + 2H_2SO_4 = C_6H_5^+ + 2HSO_4^- + H_3O^+ \quad \nu = 4$$

(5) Protonation and sulphonation

$$C_6H_5{\cdot}OH + 3H_2SO_4 = HSO_3{\cdot}C_6H_4{\cdot}OH_2^+ + 2HSO_4^- + H_3O^+ \quad \nu = 4$$

(6) Esterification and sulphonation

$$C_6H_5{\cdot}OH + 4H_2SO_4 = HSO_3{\cdot}C_6H_4{\cdot}HSO_4 + 2HSO_4^- + 2H_3O^+ \quad \nu = 5$$

Water is produced in all of these reactions except (1), and because it has a ν value of slightly less than 2 the observed ν values are expected, in these cases, to be slightly less than the integral values given above.[3]

Cryoscopic results for solutions of phenol, *p*-cresol, *o*-, *m*-, and *p*-nitrophenols, 2 : 4-dinitrophenol, and potassium *p*-nitrophenyl sulphate in sulphuric acid are given in the Table.

o- and *m*-Nitrophenol both give rather stable solutions whose freezing points decrease very slowly with time and have ν values of slightly less than 3. This suggests that either esterification (2) or mono-sulphonation (3*a*) occurs rapidly, *i.e.*, in the 10—15 minutes elapsing between the addition of the solute and the measurement of the freezing point of the solution, to give products which undergo little further reaction under the experimental conditions. Simple mono-sulphonation, which would leave an unchanged and unprotonated OH group, seems less likely than esterification. This is partly confirmed by the fact that the nitrophenol can be recovered by pouring the sulphuric acid solution on ice. Rapid hydrolysis of the phenyl hydrogen sulphate seems to be much more likely than rapid desulphonation under these conditions.

Phenol and *p*-cresol both give ν values of approximately 5, which suggests either esterification and sulphonation (6) or disulphonation (3*b*). Since we have concluded that *o*- and *m*-nitrophenol are esterified it seems reasonable to conclude that phenol and *p*-cresol are esterified and, in addition, sulphonated. The further very slow decrease in the freezing point is probably due to disulphonation.

The ν-values for *p*-nitrophenol increase from approximately 2·6 to 3·0 in a few hours and to approximately 4·0 in about 24 hr., thereafter showing only a very slight increase over a period of several days or more. *p*-Nitrophenol thus behaves rather differently from the *ortho*- and the *meta*-isomer. The initial reaction giving $\nu = 3{\cdot}0$ cannot be simply esterification since potassium *p*-nitrophenyl sulphate initially gives the expected $\nu = 3{\cdot}0$ which only increases to 3·3 during two days,

$$NO_2{\cdot}C_6H_4{\cdot}OSO_3K + H_2SO_4 = K^+ + HSO_4^- + NO_2{\cdot}C_6H_4{\cdot}O\overset{+}{S}O_3H$$

indicating that *p*-nitrophenyl hydrogen sulphate does not undergo any extensive further reaction in contrast to the product of the initial reaction of *p*-nitrophenol with sulphuric acid. It seems probable, therefore, that *p*-nitrophenol sulphonates more rapidly than the *ortho*- and the *meta*-isomer and this reaction thus competes with the esterification reaction producing a mixture of *p*-nitrobenzenesulphonic acid and *p*-nitrophenyl hydrogen sulphate. Any such mixture would give the initially observed ν-value of 3·0. The

[3] Gillespie, *J.*, 1950, 2493.

p-nitrobenzenesulphonic acid then esterifies slowly and the value of ν increases correspondingly, while the *p*-nitrophenyl hydrogen sulphate remains essentially unchanged. If the mixture formed initially contained approximately equal amounts of the hydrogen sulphate and the sulphonic acid then the esterification of the sulphonic acid would cause the value of ν to increase to 4·0, as observed. The probably more rapid rate of sulphonation of *p*-nitrophenol is of interest. Because of the conjugation between the nitro- and the hydroxyl group in *p*-nitrophenol it seems probable that it is less extensively protonated than the *ortho*- and the *meta*-isomer and is therefore correspondingly less deactivated towards sulphonation.

Freezing points of solutions of 2 : 4-dinitrophenol change very slowly with time and the ν-value obtained is about 1·3. It seems most likely that it is a weak base, *i.e.*, is partially protonated (1), and also undergoes either very slow esterification or sulphonation, or both. 2 : 4 : 6-Trinitrophenol has been shown to be a stable non-electrolyte in sulphuric acid.[2]

Experimental

Apparatus.—The apparatus and general procedure for cryoscopy have been described.[4]

Materials.—Sulphuric acid, prepared as previously described,[5] was adjusted to maximum freezing point before each experiment. Phenol and *p*-cresol were twice redistilled and had

Time (hr.)	10^2m	F. p.	ν
	Phenol		
—	0·000	10·365°	—
—	1·440	10·106	4·61
—	2·449	9·831	4·71
—	3·955	9·408	4·73
—	5·453	8·976	4·75
—	7·265	8·446	4·76
—	8·149	8·213	4·72
0·0	10·078	7·684	4·68
30·0	10·078	7·614	—
—	0·000	10·365	—
—	3·085	9·670	4·64
—	6·929	8·568	4·71
—	8·683	8·054	4·73
—	11·146	7·374	4·69
	o-Nitrophenol		
—	0·000	10·365	—
—	3·451	9·927	2·81
—	5·916	9·513	2·84
—	8·618	9·044	2·87
—	14·243	8·020	2·92
—	16,889	7·546	2·92
—	0·000	10·365	—
—	4·173	9·829	2·74
—	5·596	9·588	2·79
—	9·447	8·911	2·83
—	10·556	8·715	2·86
—	12,609	8·346	2·88
—	13·921	8·125	2·87
—	0·000	10·365	—
0·0	5·391	9·631	2·76
168·0	5·391	9·575	2·92
	m-Nitrophenol		
—	0·000	10·365	—
—	4·080	9·820	2·84

Time (hr.)	10^2m	F. p.	ν
	m-Nitrophenol		
—	7·515	9·232	2·87
—	11·071	8·617	2·87
—	13·081	8·251	2·89
—	15·214	7·892	2·87
—	0·000	10·365	—
—	3·573	9·558	2·89
—	6·434	9·186	2·88
—	8·820	8·754	2·92
—	11·380	8·321	2·90
—	13·760	7·918	2·88
0·0	16·310	7·510	2·85
24·0	16·310	7·483	2·88
—	0·000	10·365	—
—	3·066	10·006	2·74
—	5·078	9·657	2·83
—	8·349	9·092	2·87
—	10·451	8·717	2·88
—	12·916	8·239	2·94
0·0	14·891	7·957	3·01
21·0	14·391	7·953	3·01
	p-Nitrophenol		
—	0·000	10·365	—
0·18	8·644	9·160	2·63
0·43	8·644	9·154	2·64
1·90	8·644	9·107	2·74
3·22	8·644	9·017	2·90
4·1	8·644	8·964	3·00
5·0	8·644	8·796	3·32
24·5	8·644	8·415	4·05
27·7	8·644	8·372	4·15
96·0	8·644	8·340	4·19
428·0	8·644	8·332	4·21
—	0·000	10·365	—
0·13	6·619	9·497	—
2·95	6·619	9·468	2·66
5·60	6·619	9·311	3·05

Time (hr.)	10^2m	F. p.	ν
	p-Nitrophenol		
20·8	6·619	8·933	3·86
313·0	6·619	8·967	3·91
	p-Cresol		
—	0·000	10·365°	—
—	1·586	10·016	5·16
—	3·218	9·542	5·10
—	5·531	8·868	5·00
0·0	7·007	8·458	4·91
96·0	7·007	8·399	5·04
	2 : 4-Dinitrophenol		
—	0·000	10·365	—
—	10·309	9·795	1·25
—	14·267	9·438	1·31
—	18·796	9·138	1·26
—	24·537	8·746	1·22
0·0	31·902	8·238	1·20
36·6	31·902	8·018	1·31
	Potassium p-nitrophenyl sulphate		
—	0·000	10·365	—
—	3·237	9·604	3·10
—	6·362	9·076	3·01
—	9·289	8·540	3·03
0·0	1·275	7·916	3·02
17·5	1·275	7·677	3·32
—	0·000	10·365	—
0·4	5·560	9·232	2·97
3·0	5·560	9·222	3·10
25·8	5·560	9·138	3·24
50·5	5·560	9·134	3·25

[4] Gillespie, Hughes, and Ingold, *J.*, 1950, 2473.
[5] Gillespie and Oubridge, *J.*, 1956, 80.

b. p.s 179—181° and 203—205° respectively. *o*-Nitrophenol was recrystallised from alcohol–water and had m. p. 43·4—44·4°; *m*- and *p*-nitrophenol were recrystallised from dilute hydrochloric acid, m. p.s 95·0—95·5° and 112—113° respectively; 2 : 4-dinitrophenol was recrystallised from water, m. p. 112—112·5°. A sample of potassium *p*-nitrophenyl sulphate was kindly provided by Mr. C. A. Vernon.

Procedure.—In most cases, the solutions were not completely stable and their freezing points decreased slowly with time. However, except for *p*-nitrophenol this change was very slow and reasonably constant values of ν were obtained if the measurements were completed within a few hours. After a set of additions of solute the freezing point of the solution was followed over a period of time (often several days) to see if it eventually reached a constant value.

Calculations.—Values of ν, the number of moles of ions and molecules formed from one mole of the solute, were calculated from the equation

$$\nu = \theta\,(1 + 0{\cdot}0020)/(6{\cdot}12m - m_d/m)$$

where θ is the freezing-point depression calculated from the freezing point of hypothetical undissociated sulphuric acid (10·615°), m is the molality of the solute, and m_d is the molality of the products of the self-dissociation of the solvent.[6]

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1.

[*Received, March* 31*st*, 1958; *Revised, April* 28*th*, 1959.]

[6] Bass, Gillespie, and Robinson, Part XXVII, to be published.

---

564. *Optically Active Forms of* 3′ : 2″*-Dibromo*-3 : 4-5 : 6*-dibenzophenanthrene*-9 : 10*-dicarboxylic Acid, and their Stability.*

By MALCOLM CRAWFORD, R. A. M. MACKINNON, and V. R. SUPANEKAR.

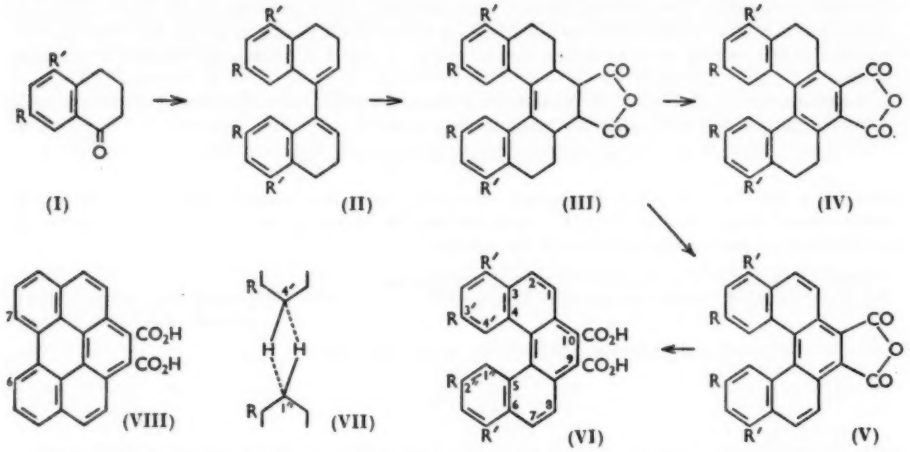
The presence of two bromine atoms enables this acid (VI; R = Br, R′ = H) to be obtained in optically active form with a half-life of 32 hr. at 22° in chloroform solution. In absence of the bromine or in presence of smaller substituents only mutarotation or partial resolution had previously been achieved. The identity of the compound has been confirmed by comparison of its ultraviolet absorption spectrum with those of compounds containing similar and related ring systems.

THE molecule of 3 : 4-5 : 6-dibenzophenanthrene is twisted into a helical shape by overcrowding.[1] Because of the resulting asymmetry Bell and Waring[2] were able to detect mutarotation in solutions of the morphine salt of 3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylic acid (VI; R = R′ = H) and partially to resolve 1′ : 3′ : 2″ : 4″-tetramethyl-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylic acid (VI; R = R′ = Me). This showed that methyl groups in the 3′ and 2″ positions decrease the rate of racemisation, presumably by interfering with the passage from one isomer to the other through the planar position. To confirm this and to obtain stable isomers an acid (VI; R = Br, R′ = H) containing larger groups, namely bromo, in the interfering 3′ and 2″ positions has been prepared. Weidlich's method[3] for the synthesis of this ring system was used with appropriate modifications.

The acid passes very readily into its anhydride. When the acid is required the orange anhydride is dissolved in hot potassium hydroxide solution giving a colourless solution, from which dilute hydrochloric acid precipitates the orange-yellow acid. After filtration and washing it can be dried under reduced pressure at room temperature. The product

[1] McIntosh, Robertson, and Vand, *J.*, 1954, 1661.
[2] Bell and Waring, *J.*, 1949, 2689.
[3] Weidlich, *Ber.*, 1938, **71**, 1203.

melts about 130° but sets again to the anhydride, m. p. 338°. The equivalent weight indicates about $\frac{1}{2}H_2O$ more than formula (VI). Reversion to the anhydride does not take place under ordinary moist atmospheric conditions but very readily on heating, recrystallising, or on dissolving in such solvents as chloroform or even acetic acid. This change was followed conveniently by observing the infrared absorption of a chloroform solution. Chloroform does not absorb between 2000 and 1600 cm.$^{-1}$; in this region the anhydride is



responsible for two characteristic peaks at 1845 and 1775 cm.$^{-1}$ respectively, whereas the acid absorbs at 1705 cm.$^{-1}$ only. The solid acid suspended in Nujol shows the latter peak, the two anhydride peaks being present only to a minute extent. In chloroform solution, however, all three are shown intensively. The acid peak at 1705 cm.$^{-1}$ vanishes on boiling the solution, indicating complete conversion into anhydride. At room temperature nearly one day is required for this peak to disappear.

The acid was resolved by use of morphine. The following procedures were used: (*a*) By working quickly so that the ethanol solution containing the morphine salts was not kept long above room temperatures, two distinct morphine salts were obtained of $[\alpha]_D^{22} = -220°$ and $+497°$ which gave respectively acids of $[\alpha]_D^{22} = -712°$ and $+745°$. (*b*) By dissolving the acid in chloroform, adding morphine suspended in chloroform, and concentrating at room temperature, four fractions of morphine salt were obtained. From the first fraction active acid of $[\alpha]_D^{25} = +589°$ and from the fourth of $[\alpha]_D^{25} = -394°$ was obtained. (*c*) By refluxing the ethanol solution of morphine salts for some time and allowing it to cool slowly only dextro-rotatory salts were obtained. Recrystallisation of the fraction of highest rotation followed by decomposition gave an acid of $[\alpha]_D^{25} = +1238°$. Obviously an asymmetric transformation had taken place in the last case resulting in extensive conversion of the lævo- into dextro-rotatory acid.

The active and partially active acids appeared to be optically stable in the solid state but racemised slowly in chloroform solution with half-lives of 32 hr. at 22° or 20 hr. at 25°. The reversion of the active acid to its anhydride in chloroform is superimposed on the racemisation. The two, however, are distinct processes as complete racemisation to zero rotation takes from 4 to 7 days whereas conversion into the anhydride is complete in less than one day. The smoothness of the decay curves in the initial stages shows that the specific rotations of anhydride and acid cannot differ widely. Anhydride formation therefore does not affect the arguments developed below about optical stability and its relationship to overcrowding in the neighbourhood of the bromine atoms. Freshly precipitated active acid is also orange-yellow. From C, H, and Br analyses after drying under

reduced pressure at room temperature the acid contains from ½ to 1 molecule of water additional to that required by formula (VI). When heated it softens at 127° but sets again to the anhydride which is orange with m. p. 338°.

It appears that by the aid of morphine partial resolution of the acid can be achieved giving both optical isomers. By asymmetric transformation the pure dextro-rotatory acid results. The nature of this transformation was not examined further as our purpose was to find the effect of large substituents on the optical stability of this overcrowded system. It is clear that the introduction of bromine into these interfering positions has the expected effect of lowering the racemisation rate. The hydrogen atoms in positions 4′ and 1″ with their considerable overlap (1·2 Å) do not seem to offer much resistance to racemisation. Substitution by methyl groups in positions 3′ and 2″ with an extra overlap of only 0·6 Å produces mutarotation in morphine salts.[2] The overlap of two bromine atoms is 1·4 Å and it brings a fair measure of optical stability. If racemisation does take

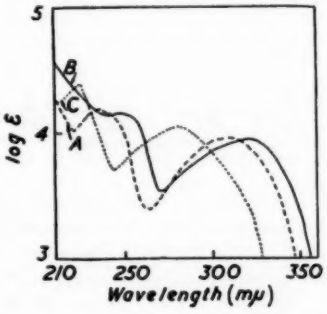


FIG. 1. *Ultraviolet spectra.*

A, Potassium 1 : 2 : 7 : 8 : 9 : 10 : 11 : 14-octahydro-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate (from high-melting anhydride) in water. $\lambda_{max.}$ 234, 239, 308 mμ ($\varepsilon_{max.}$ 15,360, 14,720, 9160); $\lambda_{min.}$ 221, 263 mμ ($\varepsilon_{min.}$ 10,750, 2450).
B, Potassium 3′ : 2″-dibromo-1 : 2 : 7 : 8 : 9 : 10 : 11 : 14-octahydro-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{max.}$ 249, 322 mμ ($\varepsilon_{max.}$ 14,400, 9000); $\lambda_{min.}$ 240, 271 mμ ($\varepsilon_{min.}$ 14,000, 3400).
C, *cis*-Stilbene (ref. 8). $\lambda_{max.}$ 224, 280 mμ ($\varepsilon_{max.}$ 24,400, 10,450).

place through a planar state it is surprising that the massive interpenetration of atoms, or alternatively the far-reaching bending of bonds necessarily occurring in that state, permits racemisation at all. It is now suggested that the transition state for racemisation of such molecules is one in which carbon atoms 1″ and 4′ are tetrahedral (VII). Some support for this is to be found in the racemisation of diaryls by tetrahedralisation of carbon.[4,5] This mechanism would require much less activation energy and would minimise atom interpenetration. It would also account for the marked effect of overlapping 3′ and 2″ substituents compared with the negligible hindrance to racemisation offered by overlapping 4′ and 1″ hydrogen atoms.

The adduct (III; R = Br, R′ = H) was first obtained in a form of m. p. 260°. Subsequent preparations had m. p. 290°. Both forms gave the same acid from which only the low-melting anhydride could be obtained. It is possible that these are *endo* and *exo* forms. Both gave the same dehydrogenation products. Weidlich [3] obtained the unsubstituted adduct (III; R = R′ = H) with m. p. 256°. In repeating this to obtain samples for comparison of ultraviolet spectra, two forms of this adduct also were obtained of m. p. 237° and 262° in about equal amounts and readily separated by their different solubilities in acetic acid. Both gave the same dehydrogenation products. Methods of structure allocation are being sought.

Ultraviolet Spectra.—The vigorous methods of dehydrogenation used in this synthesis could conceivably result in the formation of 1 : 12-benzoperylene-1′ : 2′-dicarboxylic acid (VIII) or its derivative which could not definitely be discounted by carbon and hydrogen analysis. Moreover substitution in the 6- and 7-positions of (VIII) by bromine would give rise to enantiomorphous forms. The ultraviolet absorption spectra of the compounds produced at each stage in the synthesis, however, when compared with the spectra of the

[4] Crawford and Smyth, *Chem. and Ind.*, 1954, 346.
[5] Crawford and Smyth, *J.*, 1954, 3464.

XUM

unsubstituted compounds, whose structures have been established, show that the final product (VI; R = Br, R′ = H) is not a benzoperylene derivative and allow the stages of dehydrogenation to be clearly followed. All acids were examined in the form of their potassium salts in aqueous solution, and anhydrides as potassium salts of the corresponding acids.

The two adducts (III) absorb very similarly (Fig. 1). They possess an unsaturated system resembling that of *cis*-stilbene,[6,7] but absorbing at longer wavelength with somewhat less intensity. The spectra of the two intermediate compounds (IV) also agree

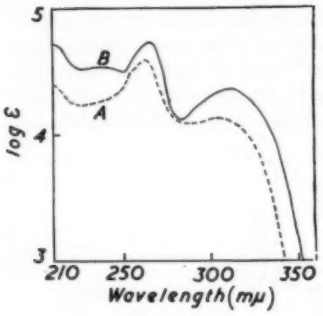


FIG. 2. *Ultraviolet spectra.*

A, Potassium 1 : 2 : 7 : 8-tetrahydro-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{max.}$ 263, 305 mμ ($\varepsilon_{max.}$ 39,200, 13,500); $\lambda_{min.}$ 288 ($\varepsilon_{min.}$ 12,600).

B, Potassium 3′ : 2″-dibromo-1 : 2 : 7 : 8-tetrahydro-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{max.}$ 266, 312 ($\varepsilon_{max.}$ 54,800, 22,900); $\lambda_{min.}$ 285 ($\varepsilon_{min.}$ 13,200).

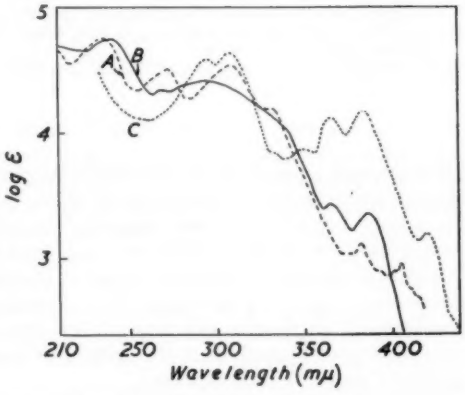


FIG. 3. *Ultraviolet spectra.*

A, Potassium 3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{max.}$ 235, 272, 310, 328, 382, 405 mμ ($\varepsilon_{max.}$ 56,000, 32,700, 34,200, 15,800, 1300, 890); $\lambda_{min.}$ 216, 253, 284, 375, 397 mμ ($\varepsilon_{min.}$ 35,800, 21,500, 19,000, 11,000, 738).

B, Potassium 3′ : 2″-dibromo-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{max.}$ 240, 270, 292, 365, 385 mμ ($\varepsilon_{max.}$ 56,000, 22,200, 26,000, 2700, 2280); $\lambda_{min.}$ 225, 264, 274, 360, 376 ($\varepsilon_{min.}$ 44,800, 20,300, 21,800, 2500, 1700).

C, Potassium 1 : 12-benzoperylene-1′ : 2′-dicarboxylate (ref. 8) in water. $\lambda_{max.}$ 295, 308, 330, 350, 365, 384, 420 mμ ($\varepsilon_{max.}$ 38,900, 43,700, 7080, 7410, 13,180, 15,140, 1580).

closely. The absorption (Fig. 2) is more intense than that of (III) owing to the 2-phenyldiphenyl system present.

The fully dehydrogenated compounds (VI) are also alike in absorption (Fig. 3) but the unsubstituted one exhibits more fine structure, possibly owing to nearer approach to uniplanarity. As all five rings are aromatic the spectra show many more peaks but are still distinct from that of the corresponding benzoperylene acid (VIII).[8]

EXPERIMENTAL

7 : 7′-*Dibromo*-3 : 3′ : 4 : 4′-*tetrahydro*-1 : 1′-*dinaphthyl* (II; R = Br, R′ = H).—Aluminium foil (8 g.) and mercuric chloride (0·5 g.) were added to a solution of 7-bromo-1-tetralone (25 g.) in dry ethanol (200 ml.) and " AnalaR " benzene (140 ml.). Dry ethanol (60 ml.) was added after 3 hours' refluxing and the cooled mixture, after a further 6 hours' refluxing, decomposed with ice-water containing hydrochloric acid. The two layers were separated, the aqueous layer

[6] Gillam and Stern, " An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," 2nd Edn., Arnold, London, 1957, p. 268.
[7] Beale and Roe, *J.*, 1953, 2755.
[8] Clar, *Ber.*, 1932, **65**, 846.

was extracted four times with benzene, and the combined benzene layers were washed successively with dilute hydrochloric acid and saturated brine. Removal of the benzene left the pinacol as a sticky brown solid which was dehydrated by four hours' boiling with acetic acid (200 ml.). On concentration of the solution the colourless crystalline *diene* (17 g.) separated, white plates, m. p. 212°, from acetic acid (Found: C, 58·0; H, 4·0; Br, 38·2. $C_{30}H_{16}Br_2$ requires C, 57·7; H, 3·9; Br, 38·4%).

3′ : 2″-*Dibromo*-1 : 2 : 7 : 8 : 9 : 10 : 11 : 14-*octahydro*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic Anhydride* (III; R = Br, R′ = H).—A solution of the foregoing diene (14 g.) and maleic anhydride (4 g.) in nitrobenzene (100 ml.) was refluxed for 3 hr. Removal of most of the solvent left a light-brown solid which was filtered off, dried thoroughly, and dissolved in hot chloroform with addition of charcoal. On addition of an equal volume of ethanol, filtering and cooling, the *anhydride* (15 g.) separated, large colourless plates, m. p. 260°, from chloroform–ethanol (Found: C, 56·0; H, 3·7; Br, 31·6. $C_{24}H_{16}O_3Br_2$ requires C, 56·0; H, 3·5; Br, 31·1%). The corresponding *acid* was precipitated on acidification of a solution of the anhydride in hot potassium hydroxide solution, m. p. 146° followed by resolidification and second m. p. 255°. In all subsequent preparations a form of the anhydride of m. p. 290° was obtained (Found: C, 56·1; H, 4·4; Br, 30·2%). The corresponding acid had m. p. 146° and second m. p. 255°. Reconversion into the anhydride gave the low-melting form.

Dehydrogenation of the foregoing anhydride. (*a*) When the anhydride, low-melting form (1 g.), and lead tetra-acetate (2 g.) in acetic acid (40 ml.) and acetic anhydride (40 ml.) were heated for 1 hr. yellow crystals separated (0·7 g.). Recrystallisation from acetic acid–acetic anhydride gave colourless prisms, m. p. 306°. This appears to be an *acetoxy-derivative* of unknown orientation (Found: C, 55·9; H, 3·5; Br, 29·2. $C_{26}H_{20}O_4Br_2$ requires C, 56·1; H, 3·6; Br, 28·8%). (*b*) The anhydride, either form (15 g.), in acetic acid was treated slowly with bromine (10 g., 2 mol.) in acetic acid and warmed. Hydrogen bromide was evolved and the colour changed to bright yellow. On concentrating and standing, 3′ : 2″-*dibromo*-1 : 2 : 7 : 8-*tetrahydro*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic anhydride* (IV; R = Br, R′ = H) crystallised out, bright yellow plates, m. p. 284°, from acetic acid (Found: C, 56·7; H, 2·6; Br, 31·2. $C_{24}H_{14}O_3Br_2$ requires C, 56·5; H, 2·7; Br, 31·1%). The corresponding acid is colourless, m. p. *ca.* 140°. (*c*) The octahydro-anhydride, either form (5 g.), in boiling acetic acid was treated slowly with bromine (6·6 g., 4 mol.) in acetic acid. Hydrogen bromide was evolved immediately and bright orange crystals quickly separated out. On 10 minutes' refluxing and cooling overnight the crystals of 3′ : 2″-*dibromo*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic anhydride* (V; R = Br, R′ = H) were filtered off and recrystallised twice from acetic anhydride, fine orange needles, m. p. 338° (Found: C, 56·8; H, 2·0. $C_{24}H_{10}O_3Br_2$ requires C, 56·9; H, 2·0%). Infrared absorption in Nujol suspension and in chloroform solution: sharp twin peaks 1845 cm.$^{-1}$ and 1775 cm.$^{-1}$.

Stability of 3′ : 2″-*Dibromo*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic Acid* (VI; R = Br, R′ = H).—The anhydride (1 g.) was boiled with potassium hydroxide solution until dissolved. To the colourless solution dilute hydrochloric acid was added until all acid was precipitated. After filtration and washing with water it was dried for 24 hr. at room temperature under reduced pressure. On standing in contact with air there was only a very slight variation in weight, possibly due to changes in humidity [Found: equiv. (after 7 days by titration), 533·7, 535·0. Calc. for $C_{24}H_{12}O_4Br_2$: equiv., 524·2]. The material consisted of orange-yellow crystals, m. p. *ca.* 130° resetting and melting again at 338°. Infrared absorption: in Nujol suspension a characteristic peak at 1705 cm.$^{-1}$; in chloroform this peak and the twin anhydride peaks appeared with equal intensity, but within 24 hr. the peak at 1705 cm.$^{-1}$ had disappeared. On one occasion when the acid was dried for 3 hr. instead of 24 hr. the peak at 1705 cm.$^{-1}$ took 40 hr. to disappear. It also disappeared immediately on boiling the chloroform solution.

1 : 2 : 7 : 8 : 9 : 10 : 11 : 14 - *Octahydro* - 3 : 4 - 5 : 6 - *dibenzophenanthrene* - 9 : 10 - *dicarboxylic Anhydride* (III; R = R′ = H).—This was prepared according to Weidlich [3] except that the solid left after removal of solvent was recrystallised from acetic acid. Two fractions were obtained of which the first after several recrystallisations from acetic anhydride gave the high-melting *anhydride*, plates, m. p. 262° (Found: C, 80·7; H, 6·0. $C_{24}H_{20}O_3$ requires C, 80·9; H, 5·7%). The second fraction treated similarly gave the low-melting *anhydride*, needles, m. p. 237° (Found: C, 80·5; H, 5·7%).

Partial Resolution of 3′ : 2″-*Dibromo*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic Acid*

—The acid (1·5 g.) suspended in boiling ethanol (50 ml.) was treated with morphine (0·91 g.). The orange-red colour faded with formation of a white precipitate, which was dissolved by adding ethanol (250 ml.) and refluxing. Cooling after filtration produced a crop of colourless crystals (0·8 g.). Concentration of the mother liquor under reduced pressure yielded three further crops. Only the first and the fourth (0·5 g.) were used.

(*a*) Several recrystallisations of the first crop from ethanol gave a morphine salt (0·22 g.), $[\alpha]_D^{22}$ (ethanol) = −220°, which on decomposition with hydrochloric acid afforded the orange-yellow *active acid* (0·12 g.), $[\alpha]_D^{22}$ (chloroform) = −712°, m. p. 330° after shrinkage at 120° representing conversion into the anhydride (Found: C, 56·9; H, 2·1. $C_{24}H_{10}O_3Br_2$ requires C, 56·9; H, 2·0%).

(*b*) Recrystallisation of the fourth crop from ethanol gave a morphine salt (0·35 g.), $[\alpha]_D^{22}$ = +497° (ethanol), which on decomposition afforded the acid (0·2 g.), $[\alpha]_D^{22}$ (chloroform) = +745°.

Racemisation.—The foregoing active acids in chloroform solution at 22° racemised with a half-life of 32 hr.:

t (hr.)	0	2¼	24	26	36	87	97
α_D	+3·28°	+2·98°	+2·08°	+1·92°	+1·52°	+0·60°	+0·49°
t (hr.)	0	13	23	49	71	95	111
α_D	−1·64°	−1·24°	−0·97°	−0·59°	−0·40°	−0·30°	−0·20°

Alternative Partial Resolution.—To the acid (1·789 g.) dissolved in chloroform morphine (1·088 g.) suspended in chloroform was added, with stirring. On concentrating the resulting solution at room temperature under reduced pressure four fractions of morphine salt were obtained. On recrystallisation and decomposition the first fraction (0·825 g.) gave the acid $[\alpha]_D^{25}$ = +589° and the last fraction (0·936 g.) gave the acid of $[\alpha]_D^{25}$ = −394°.

Asymmetric Transformation.—The acid (0·896 g.) and morphine (0·545 g.) were refluxed in ethanol (100 ml.). On cooling, four fractions of morphine salt were obtained of total weight 1·288 g. and decomposed with acid:

Fraction	1	2	3	4
Weight (g.)	0·336	0·156	0·395	0·401
$[\alpha]_D^{25}$ after recrystallisation from ethanol	+541°	—	—	—
$[\alpha]_D^{25}$ of acid obtained on decomp.	+1078°	+1150°	+1238°	+1211°

A sample of *acid* from another run was purified by reprecipitation at 10° and dried at reduced pressure. It had $[\alpha]_D^{25}$ = +1203°, m. p. 127° then 338° (Found: C, 53·8; H, 2·7; Br, 27·7. $C_{24}H_{12}O_4Br_2,H_2O$ requires C, 53·2; H, 2·6; Br, 29·5%).

Racemisation of Dextro-rotatory Acid.—A sample of active acid obtained from a transformation was allowed to racemise in chloroform solution at 25°. The half-life from the following data is 20 hr.:

t (hr.)	0	3	8	21	27	34	45	57
α_D^{25}	+3·205°	+2·902°	+2·390°	+1·523°	+1·245°	+0·967°	+0·669°	+0·418°
t (hr.)	70½	81	93	104	117	141	165	
α_D^{25}	+0·280°	+0·198°	+0·136°	+0·100°	+0·068°	+0·025°	0°	

In another racemisation in chloroform the starting solution absorbed strongly in the infrared region at 1705 cm.$^{-1}$. After 40 hr. this peak had vanished (the longer time required was due to the acid's not having been dried for so long). When fully racemised the recovered anhydride had m. p. 331° and showed the characteristic absorption peaks at 1845 and 1775 cm.$^{-1}$.

Thanks are accorded to Professor F. Bell for help.

MAKERERE COLLEGE, KAMPALA, UGANDA.
COLLEGE OF TECHNOLOGY, BELFAST (R. A. M. M.).

[*Received, November 3rd,* 1958.]

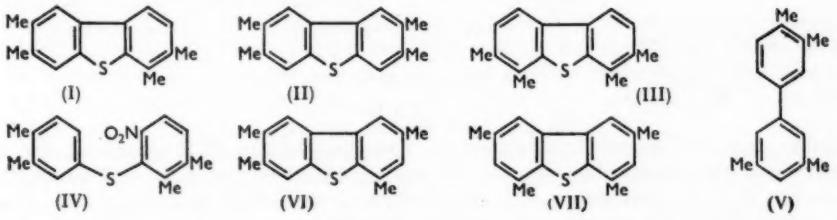
XUM

565. *The Constituents of High-boiling Petroleum Distillates. Part V.*[1] *Some Condensed Thiophen Derivatives in a Kuwait Oil.*

By W. CARRUTHERS and A. G. DOUGLAS.

1 : 2 : 6 : 7-, 1 : 3 : 6 : 7-, and 1 : 3 : 6 : 8-Tetramethyldibenzothiophen, 3-ethyl-6 : 8-dimethylnaphtho(1 : 2-*b*)thiophen, 9-thia-1 : 2-benzofluorene, and two unidentified alkyldibenzothiophens have been isolated from fractions of a Kuwait oil. The three named dibenzothiophens have been synthesised by Pschorr ring closure of the appropriately substituted 2-aminodiphenyl sulphides.

VERY little is known about the sulphur-containing compounds in high-boiling petroleum fractions. Hoog and his colleagues investigated [2] a number of gas-oil fractions boiling in the range 250—350° and concluded that they probably contained considerable amounts of condensed thiophen derivatives, and Thompson, Coleman, Rall, and Smith [3] detected condensed thiophens in a Wasson (North American) crude oil by mass-spectrometry of chromatographic fractions. So far, however, only two compounds of this type have been isolated from petroleum. 1 : 8-Dimethyldibenzothiophen was found in a Middle East oil by one of us,[4] and Richter, Williams, and Meisel [5] isolated thionaphthen from a fraction of a North American oil. We have now obtained the compounds listed in the summary from distillates of a Kuwait oil boiling above 350°.



The preparation of crystalline picrates from these distillates and the chromatographic separation of material recovered from the picrates into fractions eluted from alumina with light petroleum, benzene, and methanol were described in Part IV.[1] Further chromatography of the benzene and light petroleum eluates afforded a number of crystalline substances, several of which were identified as polycyclic aromatic hydrocarbons.[1] A number of others, however, were found to contain sulphur.

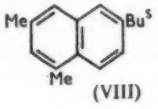
Three of these sulphur compounds were shown by their ultraviolet absorption spectra to be derivatives of dibenzothiophen, and their elementary analyses indicated the molecular formula $C_{16}H_{16}S$. One of them was converted into the known 3 : 4 : 3′ : 4′-tetramethyldiphenyl by desulphurisation with Raney nickel in boiling ethanol [6] and must therefore be represented by one of the three tetramethyldibenzothiophen structures (I), (II), or (III), each of which, of course, would afford 3 : 4 : 3′ : 4′-tetramethyldiphenyl on desulphurisation. It was identified as 1 : 2 : 6 : 7-tetramethyldibenzothiophen (I) by synthesis. 3 : 4-Dimethylthiophenol and 3-chloro-4-nitro-*o*-xylene in hot ethylene glycol solution in presence of sodium hydroxide afforded the expected nitrodiphenyl sulphide (IV) and hence by reduction of the nitro-group and Pschorr cyclisation of the amine the

[1] Part IV, *J.*, 1957, 278.
[2] Hoog, Reman, and Smithuysen, Proc. Third World Petroleum Congress, 1951, Section IV, p. 282.
[3] Thompson, Coleman, Rall, and Smith, *Analyt. Chem.*, 1955, **27**, 175.
[4] Carruthers, *Nature*, 1955, **176**, 790.
[5] Richter, Williams, and Meisel, *J. Amer. Chem. Soc.*, 1956, **78**, 2166.
[6] Blicke and Sheets, *ibid.*, 1948, **70**, 3768; 1949, **71**, 4010.

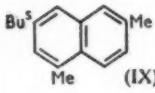
XUM

dibenzothiophen (I). The alternative cyclisation product, 1 : 2 : 5 : 6-tetramethyldibenzothiophen, was also formed in small amount. The two products were easily distinguishable since only compound (I) affords 3 : 4 : 3′ : 4′-tetramethyldiphenyl on desulphurisation. 2 : 3 : 6 : 7-Tetramethyldibenzothiophen (II) was also prepared by reaction of 2 : 2′-dihydroxy-4 : 5 : 4′ : 5′-tetramethyldiphenyl and phosphorus pentasulphide. The yield was very poor, however, and a similar approach to the 1 : 2 : 7 : 8-isomer (III) from the corresponding dihydroxydiphenyl did not yield any of the dibenzothiophen.[7] In these experiments it was noted that, whereas nitration of 3-hydroxy-*o*-xylene affords the 4-nitro-compound,[8] which can be converted into its methyl ether with diazomethane, direct nitration of 3-methoxy-*o*-xylene yields an isomer, presumably the 6-nitro-derivative.

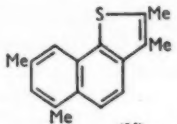
A second dibenzothiophen, $C_{16}H_{16}S$, isolated from Kuwait oil, on desulphurisation with Raney nickel likewise afforded a diphenyl derivative. There was insufficient of this material for analysis but its relative retention volume on vapour-phase chromatography under the conditions described by Beavan, James, and Johnson [9] strongly suggested that it also was a tetramethyldiphenyl. Comparison of the infrared spectrum with those of 3 : 4 : 3′ : 4′- and 3 : 5 : 3′ : 5′-tetramethyldiphenyl suggested that the desulphurisation product might be the unknown 3 : 4 : 3′ : 5′-isomer (V), and this was confirmed by the synthesis of this compound, by Dr. D. A. M. Watkins, from 3 : 4-dimethylphenylmagnesium



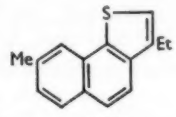
(VIII)



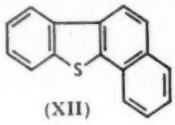
(IX)



(X)



(XI)



(XII)

Bu^s·C$_6$H$_4$·CO·CH$_2$·CHMe·CO$_2$H
(XIII)

bromide and 3 : 5-dimethyl*cyclo*hexanone. Two possibilities thus remained for the structure of the dibenzothiophen, and it was identified as the 1 : 3 : 6 : 7-tetramethyl derivative (VI) by comparison with the product of cyclisation of 2-amino-4 : 5 : 2′ : 4′-tetramethyldiphenyl sulphide. An attempt to prepare the other possible compound, 1 : 3 : 7 : 8-tetramethyldibenzothiophen, from 2-amino-2′ : 4′ : 5 : 6-tetramethyldiphenyl sulphide met with unexpected difficulties, and a mixture of products was obtained. The reaction is being further investigated.

By a similar method, a third dibenzothiophen was identified as the 1 : 3 : 6 : 8-isomer (VII). This structure followed unequivocally from the desulphurisation of the compound to 3 : 5 : 3′ : 5′-tetramethyldiphenyl, and was confirmed by synthesis from 2 : 4-dimethylthiophenol and 4-chloro-5-nitro-*m*-xylene. We are indebted to Dr. E. A. Johnson of the National Institute for Medical Research, who identified the desulphurisation product from an examination of its infrared spectrum, and by comparison with the authentic hydrocarbon which he has recently synthesised.

Two other pure crystalline alkyldibenzothiophens were isolated from picrate-forming fractions of the Kuwait oil, but because of scarcity of material we have not yet been able to identify them completely. One (m. p. 84—86°) appears to be a tri- or tetra-methyl derivative or its equivalent, and the other (m. p. 196°) a tetramethyl derivative or its equivalent.

Another compound isolated from the Kuwait oil through its crystalline picrate also had the molecular formula $C_{16}H_{16}S$ but its ultraviolet spectrum showed that it was a derivative of naphtho[1 : 2-*b*]thiophen.[10] In agreement, desulphurisation with Raney nickel afforded

[7] Cf. Gilman and Jacoby, *J. Org. Chem.*, 1938, **3**, 109; Turner and Armarego, *J.*, 1956, 1665.
[8] Holler, Huggett, and Rathmann, *J. Amer. Chem. Soc.*, 1950, **72**, 2034.
[9] Beavan, James, and Johnson, *Nature*, 1957, **179**, 490.
[10] Carruthers and Crowder, *J.*, 1957, 1932.

a naphthalene hydrocarbon $C_{16}H_{20}$ and it appeared probable from the ultraviolet absorption spectrum of this compound that the naphthalene nucleus was trisubstituted.[11] This was supported by the infrared spectrum, which suggested, further, that the substituents occupied the 1-, 3-, and 6-positions: we are very much indebted to Dr. G. Eglinton, of the University of Glasgow, for this information. The mass spectrum of the hydrocarbon, kindly determined for us by Dr. A. Quayle of Thornton Research Centre, Shell Research Ltd., showed a strong peak at mass number 183 and two weaker peaks at mass numbers 197 and 169, and afforded good evidence for the presence of a *sec.*-butyl group in the molecule. Two structures (VIII) and (IX) thus appeared likely for the desulphurisation product, bearing in mind that the *sec.*-butyl group, which must have originated in the thiophen ring of the sulphur compound, occupies a β-position in the nucleus. It was identified as 6-*sec.*-butyl-1 : 3-dimethylnaphthalene (VIII) by synthesis. Friedel–Crafts condensation of *sec.*-butylbenzene and methylsuccinic anhydride in nitrobenzene solution afforded a keto-acid regarded, by analogy,[12] as the α-methyl isomer (XIII), which was converted into the desired naphthalene by standard reactions. It follows that the sulphur compound itself must have one of the two structures (X) and (XI), and of these the latter is favoured by the results of a Kuhn–Roth estimation which indicates the presence of only three *C*-methyl groups.

In connexion with the infrared studies of naphthalene hydrocarbons which led to the recognition of the substitution pattern of the desulphurisation product and will be reported separately by Dr. Eglinton, 1 : 3-dimethyl-6-*n*-propylnaphthalene was required, and a description of its syntheses from *n*-propylbenzene and methylsuccinic anhydride is included in the Experimental section.

In separate experiments with a higher-boiling fraction of Kuwait oil than we have previously employed, chromatography and crystallisation of molecular complexes has led to the isolation of a number of crystalline substances. One of these has been identified as 9-thia-1 : 2-benzofluorene (XII) by ultraviolet absorption measurements, preparation of derivatives, and direct comparison with an authentic specimen.

The isolation of the above crystalline compounds has been facilitated to some extent by the exceptionally high sulphur content of the Kuwait oil used in the investigation. The original distillate fractions [13] of the crude oil with equivalent boiling points in the range 350—390° contained 2—3% of sulphur,[14] and many of the oily fractions obtained by crystallisation of picrates and by chromatography appeared from their ultraviolet absorption spectra to contain high proportions of sulphur compounds; derivatives of dibenzothiophen were particularly abundant. Many other crude oils have a much smaller sulphur content than the Kuwait oil and, although they may contain derivatives of condensed thiophen systems, these are probably present in smaller amounts than in the Kuwait oil and their isolation may, therefore, be correspondingly more difficult.

Experimental

Ultraviolet absorption spectra were measured in 95% ethanol with a " Unicam " spectrophotometer. M. p.s were determined on a Kofler hot stage.

Isolations from Kuwait Oil Fractions.—The particular distillates used as starting materials in this investigation were prepared in the Chemical Engineering Laboratories of the University of Birmingham under the direction of Professor F. Morton. We are very much indebted to Professor Morton for supplying us with these fractions. Their further separation by crystallisation of picrates and chromatography on alumina is described in Parts III [13] and IV.[1]

[11] Heilbronner, Frohlicher, and Plattner, *Helv. Chim. Acta*, 1949, **32**, 2479; Mosby, *J. Amer. Chem. Soc.*, 1953, **75**, 2348; Dannenberg and Dannenberg-von Dressler, *Chem. Ber.*, 1956, **89**, 1326.

[12] Berliner, " Organic Reactions," John Wiley & Sons, Inc., New York, 1949, Vol. V, p. 229; see also Carruthers and Gray, *J.*, 1958, 1280.

[13] Carruthers, *J.*, 1956, 603.

[14] Carruthers, Cerego, King, Morton, Pell, and Sagarra, Proc. Fourth World Petroleum Congress, Rome, 1955, Section V/A, paper 7.

(a) 1 : 2 : 6 : 7-*Tetramethyldibenzothiophen*. The benzene eluate (22·3 g.) obtained from the picrate of the fraction, b. p. 382·5—385°, as described in Part IV, was rechromatographed on alumina, with light petroleum (b. p. 60—80°) containing increasing proportions of benzene as eluant. Some of the fractions obtained gave crystals at −10°. Further chromatography of these and crystallisation from ethanol–benzene afforded the *dibenzothiophen* as plates, m. p. 188—189° alone or mixed with a specimen synthesised as described below (Found: C, 80·2; H, 6·6; S, 12·8. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7; S, 13·3%), $\lambda_{max.}$ 236, 241, 260, 270 (infl. 283), 294, 312, 324, 352 mμ [log ε 4·72, 4·73, 4·26, 4·30 (3·96), 4·11, 3·44, 3·35, 1·92]. The *sulphone* prepared with hydrogen peroxide in acetic acid formed prisms (in benzene), m. p. 308—309° (Found: C, 70·3; H, 5·7. $C_{16}H_{16}O_2S$ requires C, 70·6; H, 5·9%), $\lambda_{max.}$ 235, 242, 250 (infl. 276), 287, 299, 335 mμ [log ε 4·38, 4·61, 4·73 (4·08), 4·19, 4·17, 3·56]. The *s-trinitrobenzene complex* gave yellow needles, m. p. and mixed m. p. (cf. below) 184—185° (from benzene) (Found: C, 58·4; H, 4·1. $C_{16}H_{16}S,C_6H_3O_6N_3$ requires C, 58·3; H, 4·2%).

The dibenzothiophen (90 mg.) was boiled with W-5 Raney nickel [15] (2 g.) in ethanol for 12 hr., and the crude product converted into the *s*-trinitrobenzene complex. The orange prisms were separated mechanically from the mixture, and by decomposition on alumina afforded 3 : 4 : 3′ : 4′-tetramethyldiphenyl, m. p. and mixed m. p. 73—75°, $\lambda_{max.}$ 256 mμ (log ε 4·37).

(b) 1 : 3 : 6 : 7-*Tetramethyldibenzothiophen*. The light petroleum eluates of refractive index greater than 1·5000 described in Part IV were recombined and fractionally distilled under reduced pressure into 10 c.c. fractions. We thank Professor F. Morton, now of the Department of Chemical Engineering, Manchester College of Science and Technology, for having this distillation carried out, under his supervision, in his former Department at Birmingham. The fractions obtained were converted into their picrates, which were crystallised. Several of these, from fractions of equivalent b. p. 378—383°, on decomposition afforded 1 : 3 : 6 : 7-*tetramethyldibenzothiophen*, forming needles (from benzene–ethanol), m. p. 126—128° alone or mixed with a specimen synthesised as described below (Found: C, 80·2; H, 6·8. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7%), $\lambda_{max.}$ 236, 241, 260, 268, 282, 293, 315, 330, 349 mμ (log ε 4·64, 4·64, 4·31, 4·30, 3·95, 4·13, 3·41, 3·42, 2·40).

Desulphurisation of this compound (25 mg.) with Raney nickel (0·6 g.) in boiling ethanol for 6 hr. afforded an oil (20 mg.), $\lambda_{max.}$ 257—258 mμ (log ε 4·23). The infrared spectrum of distilled material was identical with that of 3 : 4 : 3′ : 5′-tetramethyldiphenyl. On vapour-phase chromatography with Apiezon M grease as stationary phase at 201°, its retention volume relative to diphenyl [9] was 7·1. The synthetic compound had relative retention volume 6·8.

(c) 1 : 3 : 6 : 8-*Tetramethyldibenzothiophen*. Four other fractions, b. p. 364°, obtained by distillation of the light petroleum eluate, gave picrates which, after crystallisation and decomposition on alumina, afforded crystalline material. Purification of this by further chromatography yielded 1 : 3 : 6 : 8-*tetramethyldibenzothiophen* as plates, m. p. 139—141° alone or mixed with an authentic specimen (Found: C, 79·7; H, 6·8. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7%), $\lambda_{max.}$ 235, 242, 258, 268, 279, 290, 320, 333 mμ (log ε 4·64, 4·64, 4·23, 4·04, 3·81, 4·05, 3·44, 3·56).

When this compound (90 mg.) was boiled with Raney nickel (1·5 g.) in ethanol for 5½ hr. an oil (75 mg.), b. p. 110°/0·4 mm. (air-bath), was obtained. It crystallised from methanol as plates, m. p. 43—45° alone or mixed with an authentic specimen of 3 : 5 : 3′ : 5′-tetramethyldiphenyl kindly provided by Dr. E. A. Johnson. It had $\lambda_{max.}$ 256 mμ (log ε 4·17). The infrared spectrum was superposible on that of the synthetic material and the retention volumes [9] relative to diphenyl determined by Dr. E. A. Johnson were 5·48 and 5·40 respectively.

(d) 3-*Ethyl*-6 : 8-*dimethylnaphtho*[1 : 2-b]*thiophen*. The light petroleum eluate ($n_D > 1·5000$) (93 g.) obtained from the picrate of the fraction of b. p. 377·5—380° (see Part IV) was re-treated with picric acid, and the picrate crystallised from ethanol–benzene and decomposed with alkali. The recovered oil (9·9 g.) partly crystallised when its solution in light petroleum was cooled to −70°. Recrystallisation from benzene–ethanol and purification through the picrate then afforded the *naphthothiophen* as plates, m. p. 150—151° (about 400 mg.) (Found: C, 80·0; H, 6·45; S, 14·0; *C*-Me, 17·65. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7; S, 13·3%), $\lambda_{max.}$ 251, 273 (infl. 290, 302, 312), 334, 350 mμ [log ε 4·44, 4·56, (3·96, 3·84, 3·50), 2·96 2·91]. The *s-trinitrobenzene complex* formed yellow needles (from benzene–ethanol), m. p. 211—213° (Found: N, 9·6. $C_{16}H_{16}S,C_6H_3O_6N_3$ requires N, 9·3%). The picrate gave red needles (from benzene), m. p. 208—209°.

The sulphur compound (100 mg.) and Raney nickel were boiled in ethanol for 6 hr. and the

[13] Adkins and Billica, *J. Amer. Chem. Soc.*, 1948, **70**, 695.

hydrocarbon obtained was purified through its *s*-trinitrobenzene complex and distilled at 120°/0·2 mm. (air-bath) (Found: C, 90·55; H, 9·25. $C_{16}H_{20}$ requires C, 90·5; H, 9·5%). It had $\lambda_{max.}$ 231, 284, 319 mμ (log ε 4·80, 3·56, 2·28). The infrared spectrum was superposable on that of 6-*sec.*-butyl-1 : 3-dimethylnaphthalene (below). The s-*trinitrobenzene complex* crystallised from benzene–ethanol as yellow needles, m. p. 114—116°, not depressed on admixture with the derivative of 6-*sec.*-butyl-1 : 3-dimethylnaphthalene (Found: C, 62·0; H, 5·4. $C_{16}H_{20},C_6H_3O_6N_3$ requires C, 62·1; H, 5·5%). The 2 : 4 : 7-trinitrofluorenone complex had m. p. 104—107° but dissociated in ethanol. The picrate was unstable.

(e) 9-*Thia*-1 : 2-*benzofluorene*. The residue from the original distillation of the Kuwait oil on the Stedman column (see Part III [13]) was further distilled under reduced pressure on a laboratory scale in the Department of Chemical Engineering, Manchester College of Science and Technology, under the supervision of Dr. P. J. King, and a fraction of corrected b. p. 390—405° was collected. After reaction with maleic anhydride this fraction (630 g.) was treated with picric acid in the usual way [1] and the oil recovered (165 g.) from the crystalline picrate was chromatographed on alumina. Fractions were eluted with light petroleum (b. p. 60—80°), benzene, and methanol. The benzene eluate (41 g.) was reconverted into the picrate which was crystallised several times from benzene–ethanol, and the recovered oil was chromatographed on alumina. Elution with light petroleum containing increasing proportions of benzene afforded a number of crystalline fractions. One of these, after further purification by chromatography gave 9-thia-1 : 2-benzofluorene (20 mg.) as colourless plates, m. p. 186—188° (from benzene–ethanol) not depressed when mixed with a specimen kindly supplied by Professor G. M. Badger (Found: C, 81·9; H, 4·4. Calc. for $C_{16}H_{10}S$: C, 82·0; H, 4·3%), $\lambda_{max.}$ 244, 252, 266, 274, 290, 302, 315, 331 (infl. 340), 347 mμ [log ε 4·58, 4·64, 4·36, 4·54, 4·13, 4·15, 3·71, 3·41 (3·01), 3·45]. The sulphone formed pale yellow needles, m. p. 232—234° (lit., 236°), and its ultraviolet absorption spectrum was identical with that recorded by Badger and Christie.[16] The s-*trinitrobenzene complex* formed yellow needles (from benzene–ethanol), m. p. 174—176° (Found: C, 59·9; H, 3·0. $C_{16}H_{10}S,C_6H_3O_6N_3$ requires C, 59·1; H, 2·9%). The 2 : 4 : 7-trinitrofluorenone complex melted at 244—246°, not 234° as recorded by Badger and Christie.[16]

(f) *Unidentified dibenzothiophen derivatives*. The light petroleum eluate (219 g.) of the picrate-forming part of the Kuwait distillate of b. p. 357·5—360° described in Part IV [1] was fractionally distilled under reduced pressure, and the fractions obtained were converted into their picrates. Two of these, from fractions, b. p. 142°/0·4 mm., by fractional crystallisation from benzene–ethanol and decomposition on alumina afforded oils which partly crystallised. The crystals (200 mg.) were collected and further purified by crystallisation of the *s*-trinitrobenzene complex. The recovered *dibenzothiophen* then formed colourless plates, m. p. 84—86° (from ethanol) (Found: C, 79·9; H, 6·4; S, 14·4. $C_{15}H_{14}S$ requires C, 79·6; H, 6·2; S, 14·2%), $\lambda_{max.}$ 231, 242 (infl. 245), 257, 268, 278, 288, 312, 323 mμ [log ε 4·52, 4·56 (4·44), 4·03, 3·98, 3·79, 3·93, 3·26, 3·38]. The s-*trinitrobenzene complex* crystallised from ethanol in yellow needles, m. p. 177° (Found: C, 57·6; H, 4·4. $C_{15}H_{14}S,C_6H_3O_6N_3$ requires C, 57·4; H, 3·9%), and the *sulphone* formed needles (from benzene), m. p. 282—284° (Found: C, 69·9; H, 5·1. $C_{15}H_{14}O_2S$ requires C, 69·7; H, 5·5%), $\lambda_{max.}$ (infl. 275) 285, 295, 325—335 mμ [log ε (3·90) 3·97, 3·93, 3·52].

The benzene eluate of the picrate-forming part of the distillate fraction of b. p. 380—382·5° (see Part IV) was chromatographed on alumina. Elution with light petroleum afforded a number of crystalline fractions. These were collected and after further purification of the crude material (83 mg.) by crystallisation of the *s*-trinitrobenzene complex, the *dibenzothiophen* derivative was obtained as plates, m. p. 196° (Found: C, 80·0; H, 6·5. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7%), $\lambda_{max.}$ 244 (infl. 260), 270, 282, 292, 311, 324 mμ [log ε 4·86, (4·30), 4·23, 3·98, 4·21, 3·50, 3·59]. The s-*trinitrobenzene complex* formed yellow needles (from ethanol–benzene), m. p. 207—209° (Found: C, 58·1; H, 4·0. $C_{16}H_{16}S,C_6H_3O_6N_3$ requires C, 58·3; H, 4·2%).

3 : 4-*Dimethylthiophenol*.—Zinc dust (34 g.) was added portionwise to a stirred ice-cold suspension of 3 : 4-dimethylbenzenesulphonyl chloride (20 g.) in 5N-sulphuric acid (200 c.c.). After 2 hr. at room temperature the mixture was boiled for 7 hr., and the thiol (11·5 g.) recovered by steam-distillation and distilled at 218°. Reaction with 1-chloro-2 : 4-dinitrobenzene in ethanol afforded the *dimethyldinitrodiphenyl sulphide* as yellow prisms, m. p. 139—140° (Found: C, 55·4; H, 4·0. $C_{14}H_{12}O_4N_2S$ requires C, 55·3; H, 4·0%).

2 : 3 : 3′ : 4′-*Tetramethyl*-6-*nitrodiphenyl Sulphide*.—A solution of 3-chloro-4-nitro-*o*-xylene

[16] Badger and Christie, *J.*, 1956, 3438.

(12·8 g.) in ethylene glycol (70 c.c.) was added to 3 : 4-dimethylthiophenol (9·5 g.) and sodium hydroxide (2·8 g.) in ethylene glycol (200 c.c.), and the mixture boiled. After ½ hr. water was added and the product extracted with benzene. Chromatography on alumina in benzene furnished the yellow *sulphide*, m. p. 74—75° (from *cyclo*hexane) (Found: C, 66·9; H, 5·95. $C_{16}H_{17}O_2NS$ requires C, 66·9; H, 6·0%).

1 : 2 : 6 : 7-*Tetramethyldibenzothiophen*.—The foregoing nitro-compound (9·0 g.) was reduced with stannous chloride (30 g.) in boiling ethanol (80 c.c.) containing hydrochloric acid (45 c.c.) for 1 hr. The resulting amine (6·0 g., b. p. 210°/5 mm.) in 25% sulphuric acid (450 c.c.) was diazotised with sodium nitrite (3 g.) in water (30 c.c.), then copper powder (10 g.) was added. Next morning the mixture was heated on the water-bath for 6 hr., and extracted with benzene. The crude product, chromatographed on alumina, afforded fractions eluted with light petroleum (b. p. 40—60°) (yield 1 g.) and with benzene (1·4 g.). The latter was recrystallised from benzene–methanol and gave 1 : 2 : 6 : 7-*tetramethyldibenzothiophen*, m. p. 192—194° not depressed when mixed with the specimen isolated from the oil which afforded 3 : 4 : 3′ : 4′-tetramethyldiphenyl on desulphurisation (Found: C, 79·5; H, 7·4. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7%). It had $\lambda_{max.}$ 236 (infl. 242, 260), 268, 292, 312, 325 mμ [log ε 4·76 (4·74, 4·23), 4·23, 4·18, 3·47, 3·49]. The *s*-trinitrobenzene complex had m. p. 178—182°, and the 2 : 4 : 7-*trinitrofluorenone complex* formed orange-red needles, m. p. 204—206° (from ethanol–benzene) (Found: C, 62·4; H, 3·6. $C_{16}H_{16}S,C_{13}H_5O_7N_3$ requires C, 62·7; H, 3·8%).

The light petroleum eluate was rechromatographed on alumina. Elution with light petroleum (b. p. 40—60°) afforded 2 : 3 : 3′ : 4′-*tetramethyldiphenyl sulphide*, m. p. 55—57° (from ethanol) (Found: C, 79·0; H, 7·6. $C_{16}H_{18}S$ requires C, 79·3; H, 7·5%), $\lambda_{max.}$ 252, 272—274 mμ (log ε 4·06, 3·77). Further elution with benzene–light petroleum (b. p. 40—60°) (1 : 10) furnished 1 : 2 : 5 : 6-*tetramethyldibenzothiophen*, m. p. 127—128° (Found: C, 80·2; H, 6·5. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7%), $\lambda_{max.}$ 241, 260, 276, 286, 317, 331 mμ (log ε 4·73, 4·17, 4·02, 4·14, 3·42, 3·58). The s-*trinitrobenzene complex* formed orange yellow needles (from benzene–ethanol), m. p. 176—178° (Found: C, 58·0; H, 4·0. $C_{16}H_{16}S,C_6H_3O_6N_3$ requires C, 58·3; H, 4·2%), and the 2 : 4 : 7-*trinitrofluorenone complex* red needles, m. p. 211—213° (Found: C, 63·1; H, 3·3. $C_{16}H_{16}S,C_{13}H_5O_7N_3$ requires C, 62·7; H, 3·8%).

4-*Methoxy*-5-*nitro*-o-*xylene*.—Concentrated nitric acid (70 c.c.) was added dropwise in ½ hr. to a stirred ice-cold solution of 4-methoxy-*o*-xylene (67 g.) in glacial acetic acid (280 c.c.). After 1 hr. the dark solution was poured into water and extracted with ether. The extract was washed with aqueous sodium hydroxide and evaporated. The crude dark oil crystallised in methanol at −10°. Recrystallisation from *cyclo*hexane afforded the *nitro-compound* (12 g.) as yellow blades, m. p. 76—78° (Found: C 59·9; H, 6·2. $C_9H_{11}O_3N$ requires C, 59·9; H, 6·2%). Further 8 g. of pure material were recovered from the mother-liquors by distillation at 120—130°/2 mm. Hydrolysis of the methoxy-compound gave the nitrophenol,[18] m. p. and mixed m. p. 85—87°.

5-*Iodo*-4-*methoxy*-o-*xylene*.—The foregoing nitro-compound was reduced catalytically with Raney nickel in ethanol. The amine formed plates, m. p. 89—90° (lit.,[17] 91°). It (19·8 g.) in 10% sulphuric acid (180 c.c.) was diazotised at 0° with sodium nitrite (24 g.) in water (50 c.c.), and a solution of potassium iodide (48 g.) in water (50 c.c.) was added. After being heated for 1 hr. on the water-bath the mixture was extracted with ether. The *iodo-compound* (21 g.) distilled at 200°/30 mm. and, crystallised from *cyclo*hexane, had m. p. 57—58° (Found: C, 41·5; H, 4·3. $C_9H_{11}OI$ requires C, 41·4; H, 4·4%). Grewe [17] gives m. p. 37° and no analysis.

2 : 2′-*Dihydroxy*-4 : 5 : 4′ : 5′-*tetramethyldiphenyl*.—Copper bronze (20 g.) was added portionwise in ½ hr. to the preceding iodo-compound (21 g.) at 200—220°, and the temperature was then raised to 260°. After ½ hr. the cooled mass was extracted with acetone. The *dimethoxydiphenyl* had b. p. 160°/0·2 mm. and formed colourless crystals (7·5 g.), m. p. 83—84° (from methanol) (Found: C, 79·8; H, 7·9. $C_{18}H_{22}O_2$ requires C, 79·95; H, 8·2%). Demethylation was effected with hydriodic acid (60 c.c.) in acetic anhydride (30 c.c.) at the b. p. for 4 hr. The *dihydroxy-compound* (6·2 g.), b. p. 200°/0·2 mm., crystallised from benzene–*cyclo*hexane in needles, m. p. 152° (Found: C, 79·1; H, 7·3. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·5%).

2 : 3 : 6 : 7-*Tetramethyldibenzothiophen*.—A mixture of the foregoing dihydroxydiphenyl derivative (1·5 g.) and phosphorus pentasulphide (0·5 g.) was slowly heated to 300° under reduced pressure (water-pump). The yellow distillate in benzene was washed with sodium

[17] Grewe, *Ber.*, 1938, **71**, 907.
[18] Diepolder, *Ber.*, 1909, **42**, 2916.

hydroxide, and the neutral gum (1·0 g.) chromatographed on alumina. Benzene–light petroleum (b. p. 60—80°) (1 : 10) eluted **2 : 3 : 6 : 7-*tetramethyldibenzothiophen*** (40 mg.), forming rods (from benzene), m. p. 211—212° (Found: C, 80·2; H, 6·4. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7%), $\lambda_{max.}$ 239 (infl. 250), 260, 269, 296 (infl. 307, 315), 326 mμ [log ε 4·94 (4·47), 4·26, 4·21, 4·32, (3·74, 3·55), 3·44]. The *sulphone*, prisms (from benzene), had m. p. 339—340° (Found: C, 70·7; H, 6·1. $C_{16}H_{16}O_2S$ requires C, 70·6; H, 5·9%), $\lambda_{max.}$ 251, 291, 303, 320, 335 mμ (log ε 4·86, 4·03, 4·04, 3·20).

3-*Methoxy*-4- *and* -6-*nitro*-o-*xylene*.—**3-*Methoxy*-4-*nitro*-o-*xylene*** was obtained from the nitrophenol [8] with diazomethane in ether–methanol as a pale yellow oil, b. p. 80—85°/0·6 mm. (air-bath) (Found: C, 59·4; H, 6·2. $C_9H_{11}O_3N$ requires C, 59·7; H, 6·1%), $\lambda_{max.}$ 270 mμ (log ε 3·68).

Nitration of 3-methoxy-*o*-xylene (7 g.) in acetic acid (30 c.c.) with concentrated nitric acid (7 c.c.) added dropwise at 0° in 1 hr. afforded only the previously unknown **6-*nitro-compound***. After chromatography on alumina in light petroleum (b. p. 60—80°) this formed yellow needles, m. p. 73—74° (from *cyclo*hexane) (Found: C, 59·8; H, 6·2. $C_9H_{11}O_3N$ requires C, 59·7; H, 6·1%), $\lambda_{max.}$ 295 mμ (log ε 3·68). Demethylation with hydriodic acid in acetic anhydride yielded the ***nitrophenol***, m. p. 123—125° (Found: C, 57·6; H, 5·2. $C_8H_9O_3N$ requires C, 57·5; H, 5·4%). The sodium salt had $\lambda_{max.}$ 415 mμ (log ε 4·2). (cf. Holler, Huggett, and Rathmann [8]).

2-*Methoxy*-3 : 4-*dimethylaniline*.—This was obtained from the above 4-nitro-compound (20 g.) by hydrogenation with Raney nickel (10 g.) in ethanol for 4 hr., and distilled at 70—75°/0·5 mm. (air-bath) (Found: C, 71·9; H, 8·8. $C_9H_{13}ON$ requires C, 71·5; H, 8·7%). The ***acetyl derivative*** gave needles, m. p. 115—116°, from aqueous acetic acid (Found: C, 68·8; H, 7·8. $C_{11}H_{15}O_2N$ requires C, 68·4; H, 7·8%).

2 : 2′-*Dihydroxy*-3 : 4 : 3′ : 4′-*tetramethyldiphenyl*.—The foregoing amine (12·7 g.) in 10% sulphuric acid (120 c.c.) was diazotised with sodium nitrite (16 g.) in water (40 c.c.). Potassium iodide (32 g.) in water (40 c.c.) was added at 0°, and reaction completed at 100° for 1 hr. The iodo-compound (13·4 g.), a red oil, b. p. 140—170° (air-bath), was treated with copper bronze (13·4 g.) as described above. The product was distilled, and the ***dimethoxydiphenyl*** (4·1 g.) collected at 170—200°/0·4 mm. (air-bath). Crystallised from ethanol, it had m. p. 95—96° (Found: C, 79·6; H, 8·5. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·2%). Demethylation (of 4·9 g.) with hydriodic acid (50 c.c.) in acetic anhydride (25 c.c.) gave the **2 : 2′-*dihydroxy*-3 : 4 : 3′ : 4′-*tetramethyldiphenyl*** (2·1 g.) as needles, m. p. 138—140° (from *cyclo*hexane) (Found: C, 79·7; H, 7·5. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·5%).

2 : 4 : 2′ : 4′-*Tetramethyl*-6-*nitrodiphenyl Sulphide*.—This compound was prepared from 4-chloro-5-nitro-*m*-xylene (2·8 g.), 2 : 4-dimethylthiophenol (2·0 g.), and sodium hydroxide (0·6 g.) in boiling ethanol (15 c.c.) in ¾ hr. After several crystallisations from ethanol–benzene the yellow ***sulphide*** had m. p. 132—133° (0·5 g.) (Found: C, 66·7; H, 5·7. $C_{16}H_{17}O_2NS$ requires C, 66·9; H, 6·0%).

1 : 3 : 6 : 8-*Tetramethyldibenzothiophen*.—The foregoing nitro-compound (0·59 g.) was reduced with stannous chloride (2·0 g.) and hydrochloric acid (3 c.c.) in boiling ethanol. The crude amine (0·35 g.) in 25% sulphuric acid (25 c.c.) was diazotised with sodium nitrite (0·2 g.) in water (2 c.c.), and copper powder (1 g.) was added. The mixture was boiled for 5 hr. and extracted with benzene. Chromatography on alumina in light petroleum (b. p. 60—80°) afforded **1 : 3 : 6 : 8-*tetramethyldibenzothiophen*** as needles, m. p. 142—143° (Found: C, 79·9; H, 6·3. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7%), $\lambda_{max.}$ 235, 242, 268, 279, 289, 320, 333 mμ (log ε 4·65, 4·62, 4·26, 4·00, 3·85, 4·13, 3·51, 3·63).

2 : 4 : 3′ : 4′-*Tetramethyl*-6′-*nitrodiphenyl Sulphide*.—A solution of 4-chloro-5-nitro-*o*-xylene (5·64 g.), 2 : 4-dimethylthiophenol (4·18 g.), and sodium hydroxide (1·25 g.) in ethylene glycol (30 c.c.) was boiled for 15 min. The cooled solution was poured into water, which was extracted with benzene, and the ***sulphide*** crystallised from light petroleum (b. p. 40—60°) as yellow prisms, m. p. 122—124° (3·97 g.). A further 2·3 g. of pure material were recovered from the mother-liquors by chromatography on alumina and elution with benzene (Found: C, 66·8; H, 5·5. $C_{16}H_{17}O_2NS$ requires C, 66·9; H, 6·0%).

1 : 3 : 6 : 7-*Tetramethyldibenzothiophen*.—The above nitro-sulphide (6·0 g.) in ethanol (140 c.c.) was boiled with stannous chloride (20 g.) and hydrochloric acid (30 c.c.) for 4 hr. The resulting crude amine (4·8 g.) in 25% sulphuric acid (300 ml.) was diazotised with sodium nitrite (3·0 g.) in water (30 c.c.). Copper powder (8·0 g.) was added and after 12 hr. at room temperature the solution was boiled for 2 hr. The product was extracted with benzene and

purified by chromatography on alumina, giving 1 : 3 : 6 : 7-*tetramethyldibenzothiophen* (440 mg.) as needles, m. p. 132·5—134·5° (Found: C, 79·8; H, 6·7%), $\lambda_{max.}$ 235, 261, 269 (infl. 284), 293, 318, 331 mμ [log ε 4·81, 4·21, 4·11 (3·89), 4·14, 3·40, 3·47]. The *sulphone* formed needles, m. p. 272—275° (from ethanol–benzene) (Found: C, 70·7; H, 5·8. $C_{16}H_{16}O_2S$ requires C, 70·6; H, 5·9%).

Reaction of sec.-*Butylbenzene with Methylsuccinic Anhydride.*—A solution of *sec.*-butylbenzene (23·8 g.) in nitrobenzene (100 c.c.) was added dropwise to a stirred ice-cold solution of methylsuccinic anhydride (18·4 g.) and aluminium chloride (45·2 g.) in nitrobenzene (200 c.c.). After 4 hr., ice and hydrochloric acid were added and nitrobenzene was removed in steam. The residue was treated with sodium carbonate solution, and the product (25 g.) obtained as an oil on acidification. Crystallisation from benzene–light petroleum (b. p. 60—80°) afforded γ-p-sec.-*butylphenyl-α-methyl-γ-oxobutyric acid* (6 g.) as needles, m. p. 108—109° (Found: C, 72·7; H, 8·2. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%). Oxidation of the acid with 30% nitric acid at 180° gave terephthalic acid (methyl terephthalate, m. p. and mixed m. p. 141—142°).

γ-p-sec.-*Butylphenyl-α-methylvaleric Acid.*—A solution of the methyl ester (prepared with diazomethane) of the preceding keto-acid (5 g.) in benzene (100 c.c.) was added dropwise to a stirred solution prepared from magnesium (0·72 g.) and methyl iodide (4·3 g.) in ether (50 c.c.) under nitrogen. The mixture was boiled for 3 hr., and the complex decomposed with dilute sulphuric acid. Extraction with sodium carbonate afforded 4-p-sec.-*butylphenyl-2-methylpentenoic acid* (2·5 g.), b. p. 130—140°/0·25 mm. (air-bath) (Found: C, 78·3; H, 8·95. $C_{16}H_{22}O_2$ requires C, 78·0; H, 9·0%). This was hydrogenated quantitatively with palladised charcoal in ethanol solution; the *valeric acid* had b. p. 140°/0·15 mm. (air-bath) (Found: C, 77·5; H, 9·8. $C_{16}H_{24}O_2$ requires C, 77·4; H 9·7%).

7-sec.-*Butyl*-1 : 2 : 3 : 4-*tetrahydro*-2 : 4-*dimethyl*-1-*oxonaphthalene.*—Stannic chloride (2·1 c.c.) in benzene (5 c.c.) was added to a cooled (ice-water) solution prepared from the valeric acid described above (2·0 g.) and phosphorus pentachloride (1·9 g.) in benzene. Next morning ice and hydrochloric acid were added and the product was extracted with benzene. The *ketone* (1·6 g.) was distilled at 120°/0·15 mm. (air-bath) (Found: C 83·5; H, 9·8. $C_{16}H_{22}O$ requires C, 83·4; H, 9·6%).

6-sec.-*Butyl*-1 : 3-*dimethylnaphthalene.*—The foregoing ketone (1·5 g.) was reduced with lithium aluminium hydride (1 g.) in ether, and the resulting alcohol (1·5 g.) heated with potassium hydrogen sulphate (0·4 g.) at 150—160° for 30 min. The dihydronaphthalene (1·1 g.) was distilled at 82—87°/0·1 mm., and dehydrogenated with palladised charcoal (0·7 g.) at 260° for 3 hr. in an atmosphere of carbon dioxide. The *naphthalene* was purified through its s-*trinitrobenzene complex* [needles, m. p. 118—119° (Found: C, 62·2; H, 5·7. $C_{16}H_{20},C_6H_3O_6N_3$ requires C, 62·1; H, 5·5%)] and obtained as an oil, b. p. 100°/0·1 mm. (air-bath) (Found: C, 90·6; H, 9·6. $C_{16}H_{20}$ requires C, 90·5; H, 9·5%), $\lambda_{max.}$ 231, 283, 318 mμ (log ε 5·07, 3·79, 2·44).

Reaction of n-*Propylbenzene and Methylsuccinic Anhydride.*—This reaction was carried out as described above, with *n*-propylbenzene (21 g.), methylsuccinic anhydride (20 g.), and aluminium chloride (49 g.) in nitrobenzene (300 c.c.). α-*Methyl-γ-oxo-γ*-p-n-*propylphenylbutyric acid* was obtained having m. p. 95—96° (from *cyclo*hexane) (Found: C, 72·2; H, 7·7. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). The *methyl ester*, prepared from the acid with diazomethane, had b. p. 180°/20 mm. (Found: C, 72·8; H, 8·3. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%). Oxidation of the acid with 40% nitric acid at 180—190° gave terephthalic acid (methyl ester, m. p. and mixed m. p. 138—140°).

α-*Methyl-γ*-p-n-*propylphenylvaleric Acid.*—A solution prepared from magnesium (1 g.) and methyl iodide (6·2 g.) in ether (80 c.c.) was added slowly to a stirred solution in benzene (100 c.c.) of the methyl ester described above (7 g.), under nitrogen. After 2 hr. the complex was decomposed with dilute sulphuric acid, and the organic layer separated and extracted with sodium carbonate. The recovered *pentenoic acid* (4·3 g.) was distilled at 130°/0·25 mm. (Found: C, 77·7; H, 9·0. $C_{15}H_{20}O_2$ requires C, 77·6; H, 8·7%). Hydrogenation of this in ethanol solution with palladised charcoal afforded the *valeric acid*, b. p. 130°/0·08 mm. (air-bath) (Found: C, 77·1; H, 9·5. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%).

1 : 2 : 3 : 4-*Tetrahydro*-2 : 4-*dimethyl*-1-*oxo*-7-n-*propylnaphthalene.*—This (2·1 g.) was obtained, as described for the *sec.*-butyl compound, from the preceding valeric acid (3·5 g.), phosphorus pentachloride (3·4 g.), and stannic chloride (3·5 c.c.) in benzene. It had b. p. 110°/0·1 mm. (air-bath) (Found: C, 83·5; H, 9·5. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%).

1 : 3-*Dimethyl*-6-n-*propylnaphthalene.*—The foregoing ketone (1·5 g.) was reduced with

lithium aluminium hydride (1 g.) in ether (200 c.c.), and the alcohol (1·5 g.) dehydrated with potassium hydrogen sulphate (0·2 g.) at 150—160° for 20 min. 1 : 2-*Dihydro*-1 : 3-*dimethyl*-6-n-*propylnaphthalene* (0·95 g.) was obtained as an oil, b. p. 80°/0·1 mm. (air-bath) (Found: C, 89·9; H, 10·1. $C_{15}H_{20}$ requires C, 89·9; H, 10·1%). This material was heated with 30% palladised charcoal at 270° for 5 hr. in an atmosphere of carbon dioxide. The *naphthalene* was isolated through its *s*-trinitrobenzene complex and distilled at 100°/0·1 mm. (air-bath) (Found: C, 90·7; H, 9·3. $C_{15}H_{18}$ requires C, 90·8; H, 9·2%). It had $\lambda_{max.}$ 231, 284, 319 mμ (log ε 4·94, 3·72, 2·43). The *s-trinitrobenzene complex* formed yellow needles (from ethanol), m. p. 98° (Found: C, 61·4; H, 5·3. $C_{15}H_{18}.C_6H_3O_6N_3$ requires C, 61·3; H, 5·2%). The 2 : 4 : 7-*trinitrofluorenone complex* gave red needles, m. p. 115—116° (Found: C, 65·25; H, 4·5. $C_{15}H_{18}.C_{13}H_5O_7N_3$ requires C, 65·5; H, 4·5%).

We are very much indebted to Dr. J. W. Cook, F.R.S., for valuable discussions, and to Dr. R. A. W. Johnstone for assistance in the vapour-phase chromatography experiments.

MEDICAL RESEARCH COUNCIL, CARCINOGENIC SUBSTANCES RESEARCH GROUP,
UNIVERSITY OF EXETER. [*Received, February 11th*, 1959.]

---

566. *Nuclear Resonance Spectra of Sulphoperamidic Acid.*

By R. E. RICHARDS and R. W. YORKE.

Line shapes and second moments have been measured for the hydrogen resonance spectra of sulphoperamidic acid crystals at 20° K, 90° K, and at room temperature. High-resolution hydrogen resonance spectra have also been obtained for a solution of this substance in dimethylformamide. It is shown that this substance both in the crystalline state and in solution in dimethylformamide exists as the zwitterion $H_3N^+O{\cdot}SO_3^-$. In the crystalline state the H–H distance is 1·72 Å with an upper limit of 1·75 Å. If ∠HNH is assumed to be tetrahedral this leads to an N–H distance of 1·06 Å with an upper limit of 1·07 Å.

SULPHOPERAMIDIC ACID can be represented in two possible ways, one of which is a zwitterion

(I) $NH_2{\cdot}O{\cdot}SO_3H$ $H_3N^+O{\cdot}SO_3^-$ (II)

Sommer *et al.*[1] favoured structure (I), regarding the acid as the amide of Caro's acid $HO{\cdot}O{\cdot}SO_3H$ on account of its strong oxidizing properties. Wannagat and Pfeiffenschneider[2] tried unsuccessfully to liberate Caro's acid by hydrolysis and by gentle oxidation of the NH_2 group with derivatives of nitrous acid. The decomposition of sulphoperamidic acid in ether suspension with diazomethane solution at −20° to +20°c did not proceed as expected; instead of $NH_2{\cdot}O{\cdot}SO_3{\cdot}CH_3$, a compound with three methyl groups all attached to the nitrogen atom was produced. Thus under mild conditions the total sulphur could be detected as sulphate. The methylated acid gave an identical *X*-ray pattern with that of the compound obtained by the union of trimethylamine oxide and sulphur trioxide which probably has the formula $(CH_3)_3N^+O{\cdot}SO_3^-$. This corresponds with the compound $C_5H_5N{\cdot}O{\cdot}SO_3$ prepared by Baumgarten and Erbe[3] from pyridine *N*-oxide and sulphur trioxide. Sulphoperamidic acid, which can be prepared from hydroxylamine and sulphur trioxide, was not therefore interpreted as the amide of Caro's acid but as the sulphur trioxide adduct to the amine oxide formula (NH_3O) of hydroxylamine. This formula was first discussed by Baumgarten and Erbe in 1938 but they finally favoured structure (I).

Further confirmation of the zwitterion formula has therefore been attempted, by

[1] Sommer, Schulz, and Nassau, *Z. anorg. Chem.*, 1925, **147**, 142.
[2] Wannagat and Pfeiffenschneider, *Naturwiss.*, 1956, **43**, 178.
[3] Baumgarten and Erbe, *Ber.*, 1938, **71**, 2603.

XUM

locating the positions of the hydrogen atoms from the hydrogen magnetic resonance spectra.

Experimental

The acid was prepared by Sommer, Schulz, and Nassau's method.[1] Pure dry ether, methanol, and chloroform were prepared by the usual methods. 30 ml. of chlorosulphuric acid were allowed to flow slowly from a dry pipette on to 13 g. of hydroxylamine sulphate. A vigorous reaction took place and when the mixture was warmed to about 100° the acid was precipitated. Heating was continued for 5 min. until the toughness of the thin paste stopped increasing. The mixture was allowed to cool in a desiccator and was then added slowly to ice-cold dry ether. The acid was made into a paste by stirring the suspension so that it could be filtered off rapidly under suction. It was washed with dry ether several times and dried in a desiccator over phosphoric oxide.

A fairly pure product is obtained directly, but to obtain a purer form, the whole mixture was dissolved with prolonged stirring in about 60 ml. of dry, ice-cold methyl alcohol, care being taken to avoid a rise in temperature. The solution was filtered and allowed to drop into 120 ml. of dry chloroform, from which stirring precipitated the pure acid as fine crystals. These were filtered off and dried in a vacuum-desiccator in which they were stored until required. The sulphoperamidic acid was found to be 98·2% pure by dropping a known weight into an excess of acidified 10% potassium iodide solution. Iodine was liberated and this was titrated against 0·1N-sodium thiosulphate solution.

The acid for the broad-line nuclear resonance experiments was transferred directly from the desiccator to a dry box and was rammed with a glass rod into a thin-walled hard-glass tube. It was then cooled in liquid oxygen and quickly sealed off.

The high-resolution nuclear resonance experiments were obtained on a saturated solution in dimethylformamide.

The hydrogen resonance spectra were obtained on the broad-line apparatus [4] at room temperature, 90° K with use of liquid oxygen as a coolant, and 20° K with use of liquid hydrogen as a coolant. The spectra on the high-resolution apparatus [5] were obtained at 27° C.

Results

The Solid.—At room temperature the nuclear resonance spectrum was very easily saturated, so the radio-frequency voltage on the coil was reduced to about 4 mv. At liquid-oxygen temperatures the sample was less easily saturated but at liquid-hydrogen temperatures a low radio-frequency voltage was required.

Fig. 1. *Derivative curve of hydrogen resonance of sulphoperamidic acid at 90° K.*

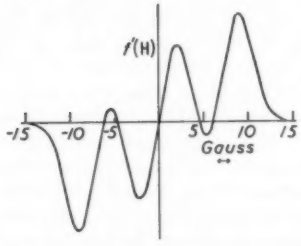
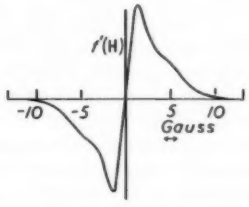


Fig. 2. *Derivative curve of hydrogen resonance of sulphoperamidic acid at 20°.*



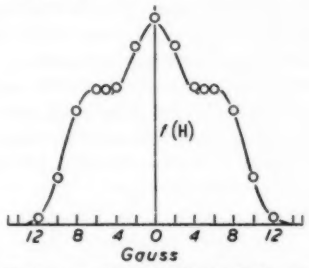
Twelve good recordings were obtained at 90° K and their mean second moment, each having been corrected for modulation broadening and for field inhomogeneity, was 28·6 gauss^2 with a standard deviation of 0·75 gauss^2. Seven of the traces were chosen whose second moment did not deviate from the mean by more than 0·5 gauss^2. A curve was then plotted by using the mean values of each of the ordinates on the seven curves (Fig. 1). The value of the modulation used is shown by the small double-headed arrow. Fig. 3 shows the absorption curve obtained by integration of the derivative curve.

[4] Richards and Smith, *Trans. Faraday Soc.*, 1951, **47**, 1261.
[5] Leane, Richards, and Schaefer, *J. Sci. Instr.*, 1959, **36**, 230.

Eight recordings at 20° K gave a mean corrected second moment of 28·4 gauss² with a standard deviation of 1·0 gauss².

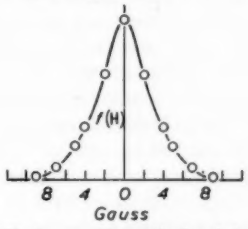
At room temperature the mean corrected second moment for seven derivative curves was 7·3 gauss² with a standard deviation of 2·1 gauss². The averaged derivative curve is shown in Fig. 2 and the corresponding absorption curve in Fig. 4.

FIG. 3. *Absorption curve of hydrogen resonance of sulphoperamidic acid at 90° K.*



Circles are theoretical points for an equilateral triangle of protons for which $\alpha = 3{\cdot}96$ gauss and $\beta^2 = 3{\cdot}74$ gauss².

FIG. 4. *Absorption curve of hydrogen resonance of sulphoperamidic acid at room temperature.*



Circles are theoretical points for an equilateral triangle of protons for which $\alpha = 3{\cdot}96$ gauss and $\beta^2 = 1{\cdot}27$ gauss² rotating about the C_3 axis.

The Solution.—The solution in dimethylformamide gave only a single broadened peak apart from the normal dimethylformamide spectrum. This peak was shifted to lower applied fields by 71 c./sec. (2·37 p.p.m.) from the single low-field proton resonance peak of the dimethylformamide.

DISCUSSION

If the acid has structure (I) then the crystal would approximate to a collection of protons in pairs, together with some relatively distant and isolated protons. In this case the absorption curve for a single proton would be superimposed upon that for a proton pair. Thus the single proton would add a central peak to the doublet of the proton-pair absorption curve and the resultant curve might have three maxima, although it is difficult to predict accurately the relative intensities of the central and outer ones. If the triplet curve does actually arise in this way then the separation of the outer maxima would correspond to the separation for a proton pair in a polycrystalline solid. This is about $2{\cdot}5\mu/x^3$ where x is the interproton distance in the pair. Since the separation of the outer maxima was 12·5 gauss an approximate value for x would be 1·12 Å. If the ∠HNH is assumed to be 120° as in urea, the N–H distance would then be 0·65 Å. This value is very much lower than any other corresponding value which has been found, and this in itself is evidence against structure (I). Further, if this very small N–H distance did occur, the second moment expected for structure (I) would be very much larger than observed.

Alternatively, if structure (I) is assumed to have the interproton distance of the pair equal to that found in urea (1·79 Å) and the third proton is 2·4 Å away (the sum of the van der Waals radii), the intramolecular second moment for this configuration would be 10·9 gauss². The intermolecular second moment in this compound could hardly be greater than 5 gauss², giving a total second moment of 16 gauss². This is very much less than the observed value. The shape and second moment of the absorption curve are therefore not consistent with structure (I).

If the substance has structure (II) and is a zwitterion then the protons would occur in groups of three at the corners of an equilateral triangle. Andrew and Bersohn [6] have

[6] Andrew and Bersohn, *J. Chem. Phys.*, 1950, **18**, 159.

calculated the theoretical line shape for this configuration and the actual line shape may be obtained by applying a Gaussian broadening function (β^2) by using the method described by Pake.[7] This takes into account the additional broadening due to the protons of neighbouring molecules, the nitrogen nuclei, the effect of finite magnitude of field modulation and the magnetic-field inhomogeneities. The theoretical points calculated for $\alpha = 3{\cdot}96$ gauss and $\beta^2 = 3{\cdot}74$ gauss^2 are shown in Fig. 3 superimposed on the observed absorption curve at 90° K. Now $\alpha = 3\mu/2d^3$, where d is the length of the side of the equilateral triangle, and in this way a value of $1{\cdot}75 \pm 0{\cdot}01$ Å is obtained for the inter-proton distance. The value of β^2 was chosen to give the best fit with the experimental curve and the sensitivity of this method is shown in previous work by Freeman and Richards [8] on potassium amide and Richards and Yorke [9] on nitroguanidine.

The measurements at 20°K showed that there was no difference within experimental error in the second moment from that at 90°K and this indicated that there is no molecular motion at 90° K. This is supported by the close agreement between the theoretical and experimental absorption curves. This close agreement also provides very strong evidence that sulphoperamidic acid has structure (II) and not structure (I).

The interproton distance of 1·75 Å derived above should be corrected for librational, stretching, and bending motions of the nuclei. Ibers and Stevenson [10] have carried out a thorough quantitative analysis of these corrections and they estimate that the liberational correction (about 2%) for the ammonium ion in various salts is about five times as important as corrections due to stretching and bending motions of the bonds. The accurate corrections require a knowledge of the frequencies of the various librational modes of the molecule in the crystal and these are not available for sulphoperamidic acid or even for glycine which is a roughly comparable example. The librational motion causes the second moment to be slightly smaller than the rigid-lattice value, so that the uncorrected N–H distance is too large. The above value may therefore be regarded as an upper limit on the distance. Kromhout and Moulton [11] made an approximate correction for librational motion in the NH_3 group in glycine from the fact that the barrier height against rotation was about 4 kcal./mole. If this correction is assumed for sulphoperamidic acid the interproton distance would be about 1·72 Å. If ∠HNH is assumed to be tetrahedral, a value of $1{\cdot}07 \pm 0{\cdot}015$ Å is obtained for the uncorrected N–H bond distance and 1·05—1·06 Å for the corrected distance. In glycine the corresponding distances were 1·07 and 1·06 Å. These distances are quite appreciably longer than the value (1·03 Å) found for the N–H distance in ammonium chloride.[10,12]

At room temperature the shape and width of the line were quite different from those at 90° K and 20° K. Since the second moment of $7{\cdot}3 \pm 2{\cdot}1$ gauss^2 was reduced to approximately a quarter of the rigid lattice value, the NH_3 group is probably undergoing rotational reorientation at a frequency greater than about 100 kc./sec. about an axis perpendicular to the plane of the protons. The shape and second moment of the derivative curve closely resemble those obtained from acetonitrile at 90° K by Gutowsky and Pake.[13] In this case the methyl group was rotating about an axis normal to the plane of the protons. Fig. 4 shows the experimental absorption curve together with the calculated points for a rotating NH_3 group, $\alpha = 3{\cdot}96$ gauss and $\beta^2 = 1{\cdot}27$ gauss^2 being used. The agreement between theory and experiment is very close and confirms that the motion occurring in this substance at room temperature is rotational reorientation about the C_3 axis.

High-resolution Experiment.—Since sulphoperamidic acid gave only a single hydrogen resonance line in solution in dimethylformamide it probably also exists in a zwitterion

[7] Pake, *J. Chem. Phys.*, 1948, **16**, 327.
[8] Freeman and Richards, *Trans. Faraday Soc.*, 1956, **52**, 802.
[9] Richards and Yorke, *Trans. Faraday Soc.*, 1958, **54**, 321.
[10] Ibers and Stevenson, *J. Chem. Phys.*, 1958, **28**, 929.
[11] Kromhout and Moulton, *J. Chem. Phys.*, 1955, **23**, 1673.
[12] Gutowsky, Pake, and Bersohn, *J. Chem. Phys.*, 1954, **22**, 643.
[13] Gutowsky and Pake, *J. Chem. Phys.*, 1950, **18**, 162.

XUM

form in this solvent. Structure (I) would have been expected to give rise to two peaks of relative intensities 2 : 1. Takeda and Jardetzky [14] have studied glycine and other amino-acids in acidic media. The NH_3 peak of glycine only appeared at high acid concentrations, since exchange took place in other solutions, but it appeared as a singlet. The broadening is not due to exchange of intermediate frequency with the solvent, but to quadrupole interaction with the nitrogen nuclei.[15] The position of the NH_3 peak of glycine was given by Takeda and Jardetzky as 964 c./sec. on a frequency scale on which the position of the aromatic protons in toluene was 1000 c./sec. and that of the methyl protons was 1197 c./sec. On this scale the centre of the triplets observed [16] in acid solution for the NH_4^+ ion occurred at 970 c./sec. and the methylammonium ion resonance [15] at 953 c./sec. The sulphoperamidic acid peak would occur at 904 c./sec. on this scale. It is therefore shifted to lower applied fields than the NH_3^+ peak for the other molecules. This would be expected since the NH_3^+ group in sulphoperamidic acid is adjacent to an oxygen atom unlike the other compounds and this would cause a further decrease in the diamagnetic shielding of the protons. It is possible, however, that changes in the bulk diamagnetic shielding, associated with changes in the solvation pattern, may also contribute to this lowering.

We thank the Department of Scientific and Industrial Research for a Maintenance Grant (to R. W. Y.), and the Hydrocarbon Research Group of the Institute of Petroleum, the Coal Board, and the Department of Scientific and Industrial Research for grants for apparatus.

PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, February 27th,* 1959.]

[14] Takeda and Jardetzky, *J. Chem. Phys.*, 1957, **26**, 1346.
[15] Roberts, *J. Amer. Chem. Soc.*, 1956, **178**, 4495.
[16] Ogg, *Discuss. Faraday Soc.*, 1954, **17**, 215.

---

567. *Quinoxaline Derivatives. Part VI.* Molecular Rearrangements of 3,4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-N-methylanilide 1-Oxide, and of Nitromalonbis-N-methylanilide.*

By J. W. CLARK-LEWIS and G. F. KATEKAR.

The *N*-oxide (I) named in the title undergoes chlorination and cyclisation to 6-chloro-1,2,3,4,2′,3′-hexahydro-4,1′-dimethyl-3,2′-dioxoquinoxaline-2-spiro-3′-indole when boiled with ethanolic hydrogen chloride, and similarly affords the 1-acetyl derivative of the spiroindole when boiled with acetyl chloride.

Usherwood and Whiteley's [1] "3,4-dihydro-4-methyl-3-oxoquinoxaline 1-oxide" is recognised as *N*-methylisatin β-oxime. Formation of this oxime from nitromalonbis-*N*-methylanilide involves a molecular rearrangement similar to that occurring in hydrolysis of 1-nitroparaffins to hydroxylamine and aliphatic acids.

USHERWOOD and WHITELEY [1] found that 3,4-dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide 1-oxide (I) undergoes a number of interesting transformations, *e.g.*, when added to sulphuric acid it gives an amine * (II; R = H), although it yields a different product when the order of mixing is reversed. They found that ethanolic hydrogen chloride converted the *N*-oxide (I) into a compound $C_{17}H_{16}O_2N_3Cl$, whereas acetyl chloride gave a compound $C_{19}H_{18}O_3N_3Cl$; no structures were proposed for these products. Both products have now been shown to contain two fewer hydrogen atoms and

* Part V, *J.*, 1957, 439.

[1] Usherwood and Whiteley, *J.*, 1923, **123**, 1069.

to be the quinoxalinespiroindoles (III; R = H and Ac). The first indications of these structures came from ultraviolet-light absorption spectra compatible with a tetrahydroquinoxaline ring system, from an N–H stretching band (in III; R = H), and from carbonyl bands at 5·94 and 5·79 μ, the latter being typical of 5-membered lactams and close to the values 5·80—5·83 μ reported [2] for some 1-methyloxindoles.

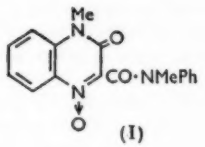
The resistance of the compounds to reducing agents [1] is understandable from the structures (III), and hydrolysis leads to steam-volatile 4-chloro-2-methylaminoaniline, which presumably is the base mistaken for *N*-methylaniline by Usherwood and Whiteley. The spiroindole (III; R = H) was inert to acetic anhydride but with acetyl chloride gave the 1-acetyl derivative (III; R = Ac). Hydrolysis of this derivative gave 4-chloro-2-methylaminoaniline and *N*-methylisatin, the latter arising from an acidic intermediate, presumably by decarboxylation and aerial oxidation of 1-methyldioxindole-3-carboxylic acid. The main product of this hydrolysis with ethanolic hydrochloric acid was, however, 6-chloro-3,4-dihydro-4-methyl-2-*o*-methylaminophenyl-3-oxoquinoxaline (II; R = Cl); this was synthesised from 4-chloro-2-methylaminoaniline and acetylisatin by the method described [3] for the parent amine (II; R = H), and for comparison the 7-chloro-isomer was likewise prepared from 5-chloro-2-methylaminoaniline. The chloro-amine (II; R = Cl) retains the bond formed in generating the indole ring, and isolation of this hydrolysis product and also *N*-methylisatin provides powerful support for the quinoxalinespiroindole structures (III; R = H and Ac). The substitution of chlorine in the 6-position of these quinoxalinespiroindoles is analogous to the conversion of 3-ethoxy-2-methylquinoxaline 1-oxide into 6-chloro-3-hydroxy-2-methylquinoxaline.[4]

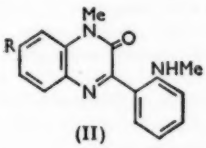
The mechanism of the formation of the quinoxalinespiroindole (III; R = H) from the *N*-oxide (I) under the influence of ethanolic hydrogen chloride is particularly interesting because the yield of product exceeds 50%, so that the *N*-oxide group apparently does not participate in both the cyclisation and the chlorination stage. Electrophilic chlorination thus seems to be excluded as formation of such a chlorinating species would consume the *N*-oxide function, and subsequent cyclisation would then be difficult to understand. Protonation of the *N*-oxide to the conjugate acid (IV) presumably is the first step, and the powerful inductive effect of the hydroxylammonium ion would then promote intramolecular electrophilic substitution at the *ortho*-position of the methylanilide by the quinoxaline 2-C-atom to give the *N*-hydroxy-compound (V). *N*-Phenylhydroxylamines when treated with hydrochloric acid yield predominantly *p*-chloro-anilines by a reaction considered to be nucleophilic [5] substitution by chloride ions, and with the intermediate (V) this leads to the isolated 6-chloro-1,2,3,4,2′,3′-hexahydro-4,1′-dimethyl-3,2′-dioxoquinoxaline-2-spiro-3′-indole (III; R = H).

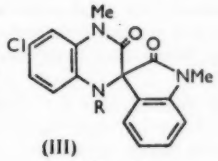
Probably the compound (V) is also an intermediate in the conversion of the *N*-oxide (I) into the amine (II; R = H). This conversion occurs in concentrated sulphuric acid, and the fact that added aromatic amines are not incorporated into the product (II; R = H) supports the assumption that reaction is intramolecular. Dilution of the sulphuric acid by these bases promotes formation of a neutral by-product which is the main product when sulphuric acid is added to the *N*-oxide instead of *vice versa*. Usherwood and Whiteley [1] formulated this neutral substance as the quinoxalinoquinoxaline (VI; R = Me or Et), which in current formulation may be written as (VII; R = Me or Et), the nature of the group R depending on the solvent used in crystallisation. The methyl and the ethyl group can be exchanged by heating with ethanol or with methanol respectively, but no exchange occurred with butan-1-ol. Detailed investigation of the structure (VII) has not been undertaken.

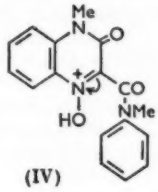
[2] Wenkert, Bose, and Reid, *J. Amer. Chem. Soc.*, 1953, **75**, 5514.
[3] Clark-Lewis, *J.*, 1957, 439.
[4] Dawson, Newbold, and Spring, *J.*, 1949, 2579.
[5] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 621; Heller, Hughes, and Ingold, *Nature*, 1951, **168**, 909.

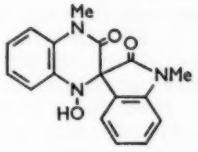
Landquist [6] has drawn attention to the discrepancy in m. p. of 3,4-dihydro-4-methyl-3-oxoquinoxaline 1-oxide (VIII) prepared by him and that reported by Usherwood and Whiteley [1] for the product obtained from nitromalonbis-*N*-methylanilide. Direct comparison has now confirmed that the two compounds are different, and Usherwood and

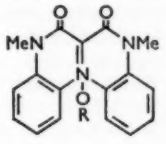

(I)

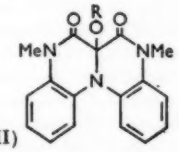

(II)

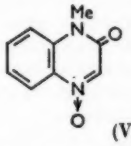

(III)


(IV)

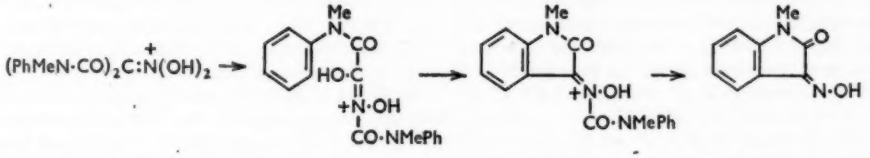

(V)


(VI)


(VII)


(VIII)

Whiteley's compound has been identified as *N*-methylisatin β-oxime by its infrared spectrum and by a mixed m. p. with the oxime prepared from *N*-methylisatin. This interesting conversion of nitromalonbis-*N*-methylanilide into *N*-methylisatin β-oxime occurs in



sulphuric acid, and appears to involve rearrangement similar to the Beckmann transformation, *e.g.*, of the protonated *aci*-nitro-compound followed by cyclisation and hydrolysis as shown. Several mechanisms [7] have been proposed for the similar rearrangement occurring in the hydrolysis of 1-nitroalkanes [8] to carboxylic acids and hydroxylamine.

Experimental

6-Chloro-1,2,3,4,2′,3′-hexahydro-4,1′-dimethyl-3,2′-dioxoquinoxaline-2-spiro-3′-indole (III; R = H).—(*a*) 3,4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide 1-oxide [1,3] (2 g.) was boiled under reflux for 2 hr. with 5% ethanolic hydrogen chloride (50 c.c.), and the solution was then evaporated under reduced pressure. Recrystallisation of the residue from ethanol gave an *ethanol solvate* (1·3 g., 61%) of the spiran as prisms, m. p. 240° raised by recrystallisation to m. p. 241—242° (Found: C, 61·5; H, 5·6; N, 11·1; Cl, 8·9. $C_{17}H_{14}O_2N_3Cl,C_2H_5\cdot OH$ requires C, 61·0; H, 5·1; N, 11·2; Cl, 9·5. Found, on material dried to constant weight at 150° over P_2O_5: C, 62·2; H, 4·3; N, 12·8; Cl, 10·3. $C_{17}H_{14}O_2N_3Cl$ requires C, 62·3; H, 4·3; N, 12·8; Cl, 10·8%), $\lambda_{max.}$ in 95% ethanol 232 (ε 35,600) and 306 mμ

[6] Landquist, *J.*, 1953, 2830.
[7] Yale, *Chem. Rev.*, 1943, **33**, 226.
[8] Hass and Riley, *ibid.*, 1943, **32**, 395.

XUM

(ε 4800), $\lambda_{min.}$ at 212 (14,600) and 280 mμ (ε 2700). When methanolic hydrogen chloride was used similarly the *N*-oxide (2 g.) gave the ***methanol solvate*** in prisms (1·2 g., 59%), m. p. 241—242° alone or when mixed with the ethanol solvate (Found: C, 60·2; H, 5·0; N, 11·4; Cl, 9·4. $C_{17}H_{14}O_3N_3Cl,CH_3{\cdot}OH$ requires C, 60·1; H, 5·0; N, 11·7; Cl, 9·9%).

(*b*) The finely powdered 1-acetyl derivative (see below) (0·5 g.) was added slowly to 92% sulphuric acid at 50°. It dissolved with effervescence and release of acetic acid (odour). The red solution was poured into water and crystallisation of the precipitate from ethanol gave prisms (0·4 g., 80%), m. p. 240° not depressed by admixture with the ethanol solvate described under (*a*).

1-Acetyl-6-chloro-1,2,3,4,2′,3′-hexahydro-4,1′-dimethyl-3,2′-dioxoquinoxaline-2-spiro-3′-indole (III; R = Ac).—(*a*) 3,4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide 1-oxide (2 g.) was heated with acetyl chloride (20 c.c.) for 1½ hr. on a steam-bath before removal of acetyl chloride under reduced pressure. The residue of ***1-acetyl derivative*** (1·2 g., 39%) crystallised from ethanol in prisms, m. p. 226—227° (Found: C, 61·8; H, 4·5; N, 11·2; Cl, 10·1. $C_{19}H_{16}O_3N_3Cl$ requires C, 61·7; H, 4·4; N, 11·4; Cl, 9·6%), $\lambda_{max.}$ in 95% ethanol 238 (ε 33,900) and 292 mμ (ε 6500), $\lambda_{min.}$ 224 (ε 21,000) and 278 mμ (ε 5900).

(*b*) The spiran (III; R = H) (1·2 g.) was boiled for 1 hr. with acetyl chloride (10 c.c.) and acetic anhydride (50 c.c.). Evaporation under reduced pressure left a residue of the 1-acetyl derivative (1 g., 83%), m. p. 225°, which crystallised from ethanol in prisms, m. p. and mixed m. p. 226°.

4-Chloro-2-methylaminoaniline Hydrochloride.—2,4-Dichloro-1-nitrobenzene (38·4 g.), pyridine (80 g.), and aqueous 25—30% methylamine (37 g.) were heated in a closed container at 100° for 28 hr. and the product was collected by filtration of the cold solution. The filtrate was evaporated under reduced pressure and the combined solid products were dissolved in the minimum quantity of 12N-hydrochloric acid. The filtered (glass wool) solution was diluted with water (*ca.* 5 l.), and the precipitate was collected; 5-chloro-*N*-methyl-2-nitroaniline [9] (24 g., 64%) crystallised from benzene–light petroleum (b. p. 60—90°) in needles, m. p. 104—105°. The nitro-amine (9·3 g.) in ethanol (100 c.c.) was hydrogenated over Raney nickel (W7) and the suspension was then filtered into 12N-hydrochloric acid (10 c.c.). The amine hydrochloride (3·6 g.) crystallised in colourless leaflets, m. p. 225—229° (decomp.), and a further crop (1·4 g.) was obtained by concentrating the mother-liquors. Crystallisation of the product (5 g., 52%) from ethanol–ether (Na-dried) gave ***4-chloro-2-methylaminoaniline hydrochloride*** in leaflets, m. p. 229° (decomp.) (Found: C, 43·6; H, 5·1; Cl, 36·8. $C_7H_{10}N_2Cl_2$ requires C, 43·5; H, 5·2; Cl, 36·7%). The hydrochloride was rapidly oxidised in water or ethanol (became red); the free base decomposed on attempted distillation under reduced pressure.

Acid-hydrolysis of 6-Chloro-1,2,3,4,2′,3′-hexahydro-4,1′-dimethyl-3,2′-dioxoquinoxaline-2-spiro-3′-indole (III; R = H).—The spiro-indole (1·5 g.) was boiled for 4 hr. with concentrated hydrochloric acid (30 c.c.) and ethanol (30 c.c.). The dark red solution was concentrated under reduced pressure, and steam-distilled after basification with aqueous sodium hydroxide. The distillate was collected in an excess of hydrochloric acid, which was then evaporated under reduced pressure. Crystallisation of the red residue from methanol–ether (Na-dried) gave 4-chloro-2-methylaminoaniline hydrochloride (0·135 g., 15%) in leaflets, m. p. and mixed m. p. 221—223° (decomp.) (Found: C, 43·4; H, 5·3; Cl, 37·0%).

Acid-hydrolysis of 1-Acetyl-6-chloro-1,2,3,4,2′,3′-hexahydro-4,1′-dimethyl-3,2′-dioxoquinoxaline-2-spiro-3′-indole (III; R = Ac).—The acetyl compound (6 g.) was boiled for 4 hr. with ethanol (120 c.c.) and concentrated hydrochloric acid (120 c.c.), then treated as above, affording 4-chloro-2-methylaminoaniline hydrochloride (0·6 g., 19%), leaflets, m. p. and mixed m. p. 225—228° (decomp.). ***6-Chloro-3,4-dihydro-4-methyl-2-o-methylaminophenyl-3-oxoquinoxaline*** (1·59 g., 33%) crystallised from the alkaline solution remaining after steam-distillation, and recrystallised from ethanol in orange needles, m. p. 188—189° not depressed by admixture with a specimen, m. p. 190—191°, synthesised as described below (Found: C, 64·0; H, 4·8; N, 13·8; Cl, 11·7. $C_{16}H_{14}ON_3Cl$ requires C, 64·1; H, 4·7; N, 14·0; Cl, 11·8%), $\lambda_{max.}$ in 95% ethanol 309 (ε 8800), 352 (ε 10,500), 368 (ε 9100), 428 (ε 6300), and 443 mμ (ε 6600); $\lambda_{min.}$ 274 (ε 5200), 329 (ε 7000), 363 (ε 8400), 389 (ε 3100), and 430 mμ (ε 2400). The alkaline filtrate from the methylaminoquinoxaline was extracted with chloroform until pale yellow and was then acidified with hydrochloric acid (red colour developed) before re-extraction with chloroform. Evaporation

[9] Blanksma, *Rec. Trav. chim.*, 1902, **21**, 273.

of the latter, orange extract left a red crystalline residue of *N*-methylisatin (0·3 g., 13%), m. p. 131° raised by recrystallisation from ethanol–water (1 : 10) to m. p. and mixed m. p. 132° (β-oxime, m. p. and mixed m. p. 190—191°).

2-o-*Aminophenyl*-6-*chloro*-3,4-*dihydro*-4-*methyl*-3-*oxoquinoxaline*.—4-Chloro-2-methylaminoaniline, from the hydrochloride (1·9 g.) and aqueous sodium acetate (1·4 g.), was heated on a steam-bath for 4 hr. with 1-acetylisatin [10] (1·9 g.) in ethanol (100 c.c.). 2-o-*Acetamidophenyl*-6-*chloro*-3,4-*dihydro*-4-*methyl*-3-*oxoquinoxaline* (0·8 g.) crystallised from the cold solution, and a further quantity (0·3 g.; total, 1·1 g., 34%) was obtained from the mother-liquors; it crystallised from ethanol in yellow needles, m. p. 264—265° (Found: C, 62·4; H, 4·3; N, 12·7; Cl, 10·2. $C_{17}H_{14}O_3N_3Cl$ requires C, 62·3; H, 4·3; N, 12·8; Cl, 10·8%). The acetyl compound (1·7 g.) was boiled with ethanol (100 c.c.) and hydrochloric acid (100 c.c.) for 4 hr. and the solution was concentrated under reduced pressure before basification with aqueous ammonia. The precipitated 2-o-*aminophenyl*-6-*chloro*-3,4-*dihydro*-4-*methyl*-3-*oxoquinoxaline* (1·1 g., 75%) crystallised from methanol in pale yellow needles, m. p. 147—148° (Found: C, 63·1; H, 4·3. $C_{15}H_{12}ON_3Cl$ requires C, 63·1; H, 4·3%).

6-*Chloro*-3,4-*dihydro*-4-*methyl*-2-o-*methylaminophenyl*-3-*oxoquinoxaline* (II; R = Cl).—The foregoing aminophenylquinoxaline (0·7 g.), toluene-*p*-sulphonyl chloride (0·56 g.), and pyridine (2·5 c.c.) were heated at 100° for 2 hr. and then poured into water. The precipitated *toluene*-p-*sulphonyl derivative* (0·9 g., 80%), m. p. 243°, crystallised from ethanol in needles, m. p. 245—246° (Found: C, 60·5; H, 4·1. $C_{22}H_{18}O_3N_3ClS$ requires C, 60·1; H, 4·1%). The sulphonanilide (0·75 g.) with methyl iodide (0·8 c.c.) and anhydrous potassium carbonate (1 g.) in acetone (10 c.c.) for 2 hr. gave the N-*methyltoluene*-p-*sulphonanilide* (0·66 g., 86%), needles (from methanol), m. p. 202—203° (Found: C, 61·4; H, 4·6. $C_{23}H_{20}O_3N_3ClS$ requires C, 60·9; H, 4·4%). This anilide (0·45 g.) was heated at 100° for 1½ hr. with 2 c.c. of a mixture of sulphuric acid (10 c.c.) and glacial acetic acid (4·5 c.c.), and the solution was diluted with water and basified with aqueous sodium hydroxide. The precipitated 6-chloro-3,4-dihydro-4-methyl-2-*o*-methylaminophenyl-3-oxoquinoxaline (0·25 g., 86%) crystallised from ethanol in orange needles, m. p. 190—191° (Found: C, 64·2; H, 4·9. Calc. for $C_{16}H_{14}ON_3Cl$: C, 64·1; H, 4·7%). It gave a colourless *N*-nitroso-derivative.

7-*Chloro*-3,4-*dihydro*-4-*methyl*-2-o-*methylaminophenyl*-3-*oxoquinoxaline*.—5-Chloro-2-methylaminoaniline was prepared by hydrogenation of the 4-chloro-*N*-methyl-2-nitroaniline, m. p. 105°, obtained from 2,5-dichloro-1-nitrobenzene and methylamine, and was converted into the quinoxaline as described for the 6-chloro-isomer: the diamine hydrochloride (5·6 g.) and acetylisatin (5·6 g.) in boiling ethanol (250 c.c.) gave 2-o-*acetamidophenyl*-7-*chloro*-3,4-*dihydro*-4-*methyl*-3-*oxoquinoxaline* (3·85 g., 41%), m. p. 243—244° (Found: C 62·4; H, 4·2; N, 12·5; Cl, 11·2. $C_{17}H_{14}O_3N_3Cl$ requires C, 62·3; H, 4·3; N, 12·8; Cl, 10·8%). Hydrolysis of the acetyl compound (1 g.) yielded 2-o-*aminophenyl*-7-*chloro*-3,4-*dihydro*-4-*methyl*-3-*oxoquinoxaline* (0·8 g., 70%) in golden needles, m. p. 195—196° (Found: C, 63·3; H, 4·2; N, 14·3; Cl, 12·4. $C_{15}H_{12}ON_3Cl$ requires C, 63·1; H, 4·2; N, 14·7; Cl, 12·4%). The base (0·55 g.) gave the *toluene*-p-*sulphonyl derivative* (0·72 g., 90%), yellow needles (from ethanol), m. p. 230° (Found: C, 59·8; H, 4·1. $C_{22}H_{18}O_3N_3ClS$ requires C, 60·1; H, 4·1%), and with methyl iodide gave the N-*methyltoluene*-p-*sulphonanilide* (74%), prisms, m. p. 215—216° (Found: C, 60·7; H, 4·5. $C_{23}H_{20}O_3N_3ClS$ requires C, 60·8; H, 4·4%). Hydrolysis of this derivative (0·3 g.) then yielded 7-*chloro*-3,4-*dihydro*-4-*methyl*-2-o-*methylaminophenyl*-3-*oxoquinoxaline* (0·15 g., 80%), orange needles, m. p. 165° (Found: C, 64·4; H, 4·7; N, 13·4. $C_{16}H_{14}ON_3Cl$ requires C, 64·1; H, 4·7; N, 14·0%).

3,4-*Dihydro*-4-*methyl*-3-*oxoquinoxaline*-2-*carboxy*-N-*methylanilide* 1-*Oxide and its Behaviour with Sulphuric Acid in the Presence of Bases*.—(*a*) The *N*-oxide [1,3] (I) (3 g.) gave 1,2-dihydro-1-methyl-3-*o*-methylaminophenyl-2-oxoquinoxaline [3] (1·8 g., 69%), m. p. 131—133°, when stirred with 92% sulphuric acid (10 c.c.). This, in 95% ethanol, had $\lambda_{max.}$ 296 (ε 8400), 350 (ε 8700), 366 (ε 7600), and 440 mμ (ε 5400), $\lambda_{min.}$ 272 (ε 4800), 326 (ε 5800), 362 (ε 6700), and 389 mμ (ε 3600), and an inflexion at 420 mμ (ε 4900).

(*b*) The *N*-oxide (0·5 g.) was finely powdered and slowly added to a mixture of 92% sulphuric acid (5 c.c.) and ethylaniline (3 c.c.) which was stirred and warmed to effect dissolution before being poured into water. The precipitate (A) was collected and basification of the filtrate and removal of ethylaniline in steam gave the methylaminophenylquinoxaline (0·18 g., 42%);

[10] Suida, *Ber.*, 1878, **11**, 585.

crystallisation of half the product from ethanol gave prisms of 1,2-dihydro-1-methyl-3-*o*-methylaminophenyl-2-oxoquinoxaline, m. p. and mixed m. p. 133°, and the other half after chromatography on alumina (single band) with benzene gave needles, m. p. 135°, from ethanol. The precipitate (A) crystallised from ethanol in pale yellow needles, consisting of 2-ethoxy-3,4,3′,4′-tetrahydro-4,4′-dimethyl-3,3′-dioxo-2*H*-quinoxalino(1′,2′:1,2)quinoxaline (0·2 g., 36%), m. p. 239° alone and when mixed with the compound described below.

(*c*) These reagents with *N*-oxide (0·5 g.) similarly gave the *o*-methylaminophenylquinoxaline (0·2 g., 47%), m. p. and mixed m. p. 135°, which was homogeneous when chromatographed, together with the quinoxalinoquinoxaline (0·17 g., 31%), m. p. 242°.

(*d*) With sulphuric acid and *NN*-dimethylaniline the *N*-oxide gave results similar to those described under (*b*) and (*c*).

2-*Ethoxy*-3,4,3′,4′-*tetrahydro*-4,4′-*dimethyl*-3,3′-*dioxo*-2H-*quinoxalino*(1′,2′:1,2)*quinoxaline* (VII; R = Et).—92% Sulphuric acid (0·5 c.c.) was added to the *N*-oxide (0·3 g.), which dissolved with slight effervescence to form a bright red solution.[1] The solutions from seven such experiments were poured into water (200 c.c.), and the yellow precipitate was treated with chloroform–ethanol. Crystallisation gave the *quinoxalinoquinoxaline* in pale yellow prisms (1·4 g., 60%), m. p. 243° (Found: C, 67·7; H, 5·7; N, 12·5; OEt, 11·6. $C_{19}H_{19}O_3N_3$ requires C, 67·6; H, 5·7; N, 12·5; OEt, 13·4%). A small quantity of the amine (II; R = H) was obtained as a by-product.

3,4,3′,4′-*Tetrahydro*-2-*methoxy*-4,4′-*dimethyl*-3,3′-*dioxo*-2H-*quinoxalino*(1′,2′:1,2)*quinoxaline* (VII; R = Me) was obtained by the method used for the ethoxy-analogue except that the precipitate was treated with chloroform–methanol. Crystallisation gave pale yellow prisms (1·38 g., 60%), m. p. 276—278° (Found: C, 66·6; H, 5·3; N, 13·0. $C_{18}H_{17}O_3N_3$ requires C, 66·9; H, 5·3; N, 13·0). When boiled with ethanol (25 c.c.) for 2 hr. the methoxy-compound (0·5 g.) gave the ethoxy-analogue (0·45 g., 90%), m. p. and mixed m. p. 243—244°. Neither compound exchanged its alkyl group with butan-1-ol under similar conditions.

Nitromalonbis-N-*methylanilide*.—Nitric acid (*d* 1·44; 2 c.c.) was added to a solution of hydroxyiminomalonbis-*N*-methylanilide (5 g.) in chloroform (30 c.c.), and the mixture was heated to the b. p. and then allowed to evaporate spontaneously to a syrupy liquid. Ethanol (30 c.c.) was added and the precipitated nitro-compound (2·4 g., 46%) was collected; it crystallised from aqueous methanol (charcoal) in colourless elongated prisms, m. p. 155—156° (Found: C, 62·7; H, 5·1; N, 12·8. Calc. for $C_{17}H_{17}O_4N_3$: C, 62·4; H, 5·2; N, 12·8%).

N-*Methylisatin* β-*Oxime from Nitromalonbis*-N-*methylanilide*.—Finely powdered nitromalonbis-*N*-methylanilide (4 g.) was added slowly to 92% sulphuric acid (30 c.c.), and the deep red solution was warmed gently until evolution of carbon dioxide (lime-water) ceased. The cooled mixture was added to water (300 c.c.), and the product (1·4 g., 65%), which separated slowly, was collected; the oxime crystallised from water in bright yellow needles, m. p. 192°, which changed their crystal form when dried at 120° over phosphoric oxide (Found: C, 61·1; H, 4·7; N, 15·8. Calc. for $C_9H_8O_2N_2$: C, 61·4; H, 4·6; N, 15·9%). It was insoluble in aqueous sodium carbonate but soluble in aqueous sodium hydroxide, and showed an O–H band at 3560 cm.$^{-1}$ and a carbonyl band at 1725 cm.$^{-1}$. The oxime prepared in this way was reported [1] to be 3,4-dihydro-4-methyl-3-oxoquinoxaline 1-oxide (VIII), but a mixture of the authentic *N*-oxide [6] (m. p. 208—209°) with the oxime melted at 150—156°. The product from nitromalonbis-*N*-methylanilide was indistinguishable from the oxime [11] prepared from *N*-methylisatin.[12]

The authors thank Mr. A. G. Moritz for infrared measurements and Dr. J. K. Landquist for a gift of 3,4-dihydro-4-methyl-3-oxoquinoxaline 1-oxide. Microanalyses were performed in the C.S.I.R.O. Microanalytical Laboratories, and Dr. Zimmermann reports that many of our compounds were unusually difficult to burn for nitrogen analysis.

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, March* 10*th*, 1959.]

[11] Borsche and Sander, *Ber.*, 1914, **47**, 2823.
[12] Borsche and Jacobs, *ibid.*, p. 361.

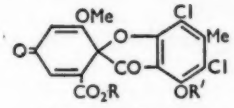
568. *The Constitution of Geodoxin, a Metabolic Product of* Aspergillus terreus *Thom.*

By C. H. Hassall and T. C. McMorris.

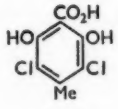
Geodoxin, $C_{17}H_{12}O_8Cl_2$, has been isolated from the culture fluid of *Aspergillus terreus* Thom. Degradation experiments lead to the constitution (IX). The relation of this structure to those of geodin and erdin is discussed.

The metabolic products of *Aspergillus terreus* Thom (Ac.100) were first investigated by Raistrick and his collaborators [1a] in connection with the ability of certain fungi to assimilate chlorine from culture solutions containing chloride ion. The two chlorinated metabolites geodin and erdin, which were isolated from the culture fluids of this species and *A. terreus* Thom (Ac.45), have been the subject of an interesting series of investigations.[1a-d,2] As a result, the structures (Ia) and (II) have been assigned to geodin and erdin respectively. We have found that a culture of the strain Ac.100 lost the capacity to synthesise geodin but acquired the ability to produce a new chlorinated metabolite. This was, presumably, the result of spontaneous mutation favoured by the conditions of subculturing. The new compound, which we name geodoxin, has been studied with the expectation that elucidation of its structure would contribute to our understanding of the catabolism or biogenesis of geodin and erdin.

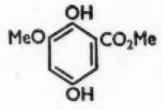
Geodoxin, $C_{17}H_{12}O_8Cl_2$, is not optically active. It has phenolic properties which include insolubility in sodium hydrogen carbonate solution but solubility in dilute, aqueous sodium hydroxide. Analytical evidence indicates one active hydrogen atom and one *C*-methyl and two methoxyl groups. Pyrolysis readily affords 2,4-dichloro-orcinol (4,6-dichloro-5-methylresorcinol); dichloro-*p*-orsellinic acid (III) is produced by oxidation with hydrogen peroxide in alkali.



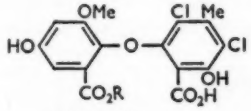
(Ia) R = Me, R′ = H
(Ib) R = R′ = Me
(II) R = R′ = H



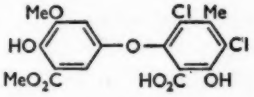
(III)



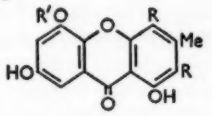
(IV)



(V) R = H
(VI) R = Me



(VII)



(VIIIa) R = Cl, R′ = Me
(VIIIb) R = R′ = H

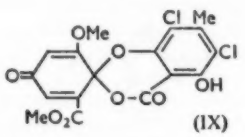
In the presence of palladium–charcoal, geodoxin absorbs two atoms of hydrogen very rapidly. The product, dihydrogeodoxin, dissolves in sodium hydrogen carbonate solution and can be titrated as a monobasic acid. It gives an intense violet colour with ferric chloride, contains two methoxyl groups, and with diazomethane affords a neutral compound containing five methoxyl groups. Dihydrogeodoxin is hydrolysed by alkali to a dibasic acid, $C_{16}H_{12}O_8Cl_2$, containing a single methoxyl group. These properties of dihydrogeodoxin, and its infrared and ultraviolet absorption spectra, require one methoxycarbonyl,

[1] (*a*) Raistrick and Smith, *Biochem. J.*, 1936, **30**, 1315; (*b*) Clutterbuck, Koerber, and Raistrick, *ibid.*, 1937, **31**, 1089; (*c*) Calam, Clutterbuck, Oxford, and Raistrick, *ibid.*, 1939, **33**, 579; (*d*) *Idem*, *ibid.*, 1947, **41**, 458.
[2] Barton and Scott, *J.*, 1958, 1767.

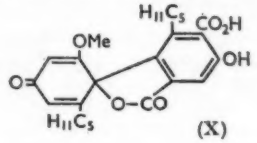
one carboxyl, one methoxyl, and two phenolic hydroxyl groups. The remaining oxygen atom may be attributed to a bridge in a substituted diphenyl ether. To test this possibility, dihydrogeodoxin was treated with 80% sulphuric acid: dichloro-orcinol, a high-melting compound, $C_{15}H_{10}O_5Cl_2$, and methyl 2,5-dihydroxy-3-methoxybenzoate (IV) were isolated from the reaction mixture. This result, taken with the evidence of a dichloro-*p*-orsellinic acid unit in geodoxin, indicates structure (VI) or (VII) for dihydrogeodoxin.

The structures (V) and (VI) correspond to those assigned by Barton and Scott [2] to erdin and geodin hydrates, compounds obtained by mild treatment of geodin and erdin with 80% sulphuric acid. The structure (VII) for dihydrogeodoxin has been excluded by showing that erdin hydrate and the dibasic acid obtained by hydrolysis of dihydrogeodoxin are identical. The high-melting by-product, $C_{15}H_{10}O_5Cl_2$, contained one methoxyl group and showed ultraviolet and infrared characteristics indicative of a xanthone. It must be formulated as (VIIIa), being produced unambiguously from the sequence: ester hydrolysis, decarboxylation, and ring closure. This structure is related to that proposed [2] for norgeodin A (VIIIb) which is formed when geodin (Ia) is treated with hydriodic acid.

The structure of dihydrogeodoxin, the fact that this acid is formed very readily by hydrogenolysis of geodoxin, a compound with phenolic properties but with no free carboxyl group, and the evidence of a single active hydrogen atom in geodoxin leads to the structure (IX) for this compound. There is spectroscopic evidence in support of this formulation. The carbonyl frequencies in the infrared absorption spectrum are readily explained. In particular, a band near 1670 cm.$^{-1}$, which also occurs in the spectra of geodin, erdin, and picrolichenic acid,[3] is attributed to a doubly conjugated carbonyl group in a six-membered ring. Since the aromatic and the cyclohexadienone ring are not in conjugation, the sum of the contributions of these individual chromophores should account for the absorption spectrum of geodoxin. A curve obtained by subtracting the spectrum of dichloro-*p*-orsellinic acid (III) from that of geodoxin has $\lambda_{max.}$ 230, 275 mμ (log ε 4·35,

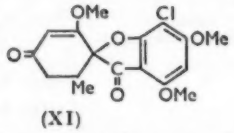


(IX)

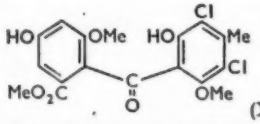


(X)

3·9). There is a remarkable similarity to the curve with $\lambda_{max.}$ 235, 280 mμ (log ε 4·4, 3·8) obtained by subtracting the absorption spectrum of orsellinic acid from that of picrolichenic acid (X). The curves show a similarity to that of a 5-methoxycyclohexa-2,5-dienone derivative prepared by Jeger and his co-workers.[4]



(XI)



(XII)

Recent studies support the suggestion that the biogenesis of griseofulvin (XI) involves the linkage of " acetate units " to form a benzophenone derivative which may, in turn, be converted by oxidative coupling into a spiran.[5,6] There is no direct evidence on the biogenesis of the related compounds geodin and erdin although Scott [6] has shown that geodin methyl ether (Ib) is formed from the related 2,4′-dihydroxybenzophenone derivative (XII) by oxidative coupling *in vitro*. Comparison of the structures of geodin and geodoxin suggests that the latter compound may be synthesised in Nature from geodin either directly

[3] Wachtmeister, *Acta Chem. Scand.*, 1958, **12**, 147.
[4] Jeger, Ruegg, and Ruzicka, *Helv. Chim. Acta*, 1947, **30**, 1294.
[5] Birch, Blance, and Smith, *J.*, 1958, 4582.
[6] Scott, *Proc. Chem. Soc.*, 1958, 195.

by a Baeyer–Villiger-type oxidation,[7] such as has been indicated in other metabolic sequences,[8] or indirectly by formation of geodin hydrate followed by oxidative coupling. We are seeking further evidence on the mode of biogenesis of geodoxin.

Experimental

M. p.s were determined by means of a Kofler block. Ultraviolet spectra were determined in ethanol on a Beckman spectrophotometer, model D.U. Infrared spectra, for which we are grateful to Dr. S. M. Nagy, Massachusetts Institute of Technology, and Dr. H. E. Hallam and Mr. D. Jones, University College of Swansea, were measured for potassium bromide discs unless otherwise stated. Microanalyses were carried out by Dr. F. Pascher, Bonn, Germany.

Isolation of Geodoxin.—Czapek–Dox agar slopes of *Aspergillus terreus* Thom (Ac.100) which had been growing for 14 days were used to inoculate sterilised Czapek–Dox medium (Raistrick and Smith [1a] modification) in flat-sided bottles of approximately 1 l. capacity. One slope was used to inoculate four bottles. The bottles were kept at 28—30°. After five weeks the dark brown culture fluid was separated from mycelium. The fluid (10 l. batch) was adjusted to pH 6·6 and stirred with activated charcoal (100 g.) for 1 hr. The charcoal was separated by filtration, dried, and extracted with methanol (3 × 1·5 l.). The methanol extract was concentrated in vacuo at 35—40° to 500 c.c. and left in a refrigerator. During two days *geodoxin* (225 mg.) separated as yellow crystals. It crystallises from chloroform–ether or ethyl acetate–light petroleum (b. p. 60—80°) as yellow needles, m. p. 216—217° (decomp.) [Found: C, 49·3; H, 3·00; O, 31·0; Cl, 16·1; *C*-Me, 3·7; OMe, 15·5; active H, 0·31%; *M* (Rast), 375. $C_{17}H_{12}O_8Cl_2$ requires C, 49·2; H, 2·9; O, 30·8; Cl, 17·1; 1*C*-Me, 3·6; 2OMe, 14·9; active H, 0·24%; *M*, 415], $[\alpha]_D$ 0° (*c* 1·0 in chloroform), $\lambda_{max.}$ 270, 345 mμ (log ε 3·95, 3·73). The subtraction curve geodoxin — dichloro-*p*-orsellinic acid [$\lambda_{inflex.}$ 250, $\lambda_{min.}$ 277 mμ (log ε 3·85, 2·3)] gave $\lambda_{max.}$ 230, 275 mμ (log ε 4·35, 3·9). The infrared spectrum in chloroform showed bands at 3250 (OH), 1735 (lactone and CO_2Me), and 1672 cm.$^{-1}$ (conjugated CO).

Degradation of Geodoxin.—(a) *Pyrolysis.* Geodoxin (40 mg.) was heated to 200°/1 atm. until no more sublimate was formed. This product was resublimed (60°/0·1 mm.), to yield needles, m. p. and mixed m. p. with 2,4-dichloro-orcinol, 166—168°.

(b) *By alkaline hydrogen peroxide.* Geodoxin (105 mg.) in N-sodium hydroxide (2 c.c.) was treated with 30% hydrogen peroxide (2·5 c.c.). After 2 hr. further sodium hydroxide (4 c.c.) and hydrogen peroxide (5 c.c.) were added. The mixture was set aside for 2 days during which the solution became colourless. Acidification gave a precipitate (20 mg.) which was purified by sublimation at 100° in a high vacuum, to give crystals, m. p. and mixed m. p. with dichloro-*p*-orsellinic acid, 217° (Found: C, 41·0; H, 2·6; O, 26·6; Cl, 30·0. Calc. for $C_8H_6O_4Cl_2$: C, 40·5; H, 2·5; O, 27·0; Cl, 30·0%).

The dichloro-*p*-orsellinic acid which was used for comparison was prepared by the following unambiguous route. 2,6-Dihydroxy-4-methylbenzoic acid was converted into its methyl ester by refluxing it with dimethyl sulphate, sodium hydrogen carbonate, and acetone, followed by working up in the usual way. A saturated solution of chlorine in carbon tetrachloride was added to the ester at 0° until the yellow colour persisted. Next morning the excess of chlorine and carbon tetrachloride were removed. The product, m. p. 166—167° (from ethanol), was converted into *dichloro*-p-*orsellinic acid* (*3,5-dichloro-2,6-dihydroxy-4-methylbenzoic acid*) by refluxing it for 3 hr. in 0·5N-sodium hydroxide to which ethanol (50% by volume) had been added. Working up in the usual way and recrystallisation from acetic acid gave the acid, m. p. 217° (decomp.) (Found: C, 40·5; H, 2·3; Cl, 29·6. $C_8H_6O_4Cl_2$ requires C, 40·2; H, 2·5; Cl, 29·7%).

Dihydrogeodoxin.—Geodoxin (300 mg.), in ethanol, was shaken with hydrogen in the presence of palladium–charcoal (0·9 g.). Uptake of hydrogen (0·98 mol.) was complete in 30 sec. The product crystallised from ethyl acetate–light petroleum (b. p. 60—80°) as white prisms, m. p. 203—206° (decomp.) (Found: C, 49·4; H, 3·4; O, 30·3; Cl, 16·8; OMe, 15·2%; equiv., 402. $C_{17}H_{14}O_8Cl_2$ requires C, 49·0; H, 3·4; O, 30·7; Cl, 17·0; 2OMe, 15·9%; equiv. for a monobasic acid, 417). Dihydrogeodoxin dissolves readily in sodium hydrogen carbonate solution. The solution in ethanol gives a purple colour with ferric chloride.

[7] Hassall, *Org. Reactions*, 1957, **9**, 73.
[8] Eppstein, Meister, Murray, and Peterson, *Vitamins and Hormones*, 1956, **14**, 394.

XUM

Dihydrotrimethylgeodoxin, m. p. 121°, was obtained in admixture with another unidentified methylation product, m. p. 151°, when dihydrogeodoxin was treated with dimethyl sulphate and sodium hydroxide solution. The lower-melting compound was found, by mixed m. p. determination and comparison of infrared spectra, to be trimethylerdin hydrate, m. p. 121°, $\lambda_{max.}$ 314 mμ (log ε 3·7).

Reactions of Dihydrogeodoxin.—(a) *With sodium hydroxide.* Dihydrogeodoxin (100 mg.) was refluxed with ethanol (15 c.c.) and N-sodium hydroxide (7·5 c.c.) for 1 hr. Acidification followed by removal of ethanol under reduced pressure afforded a precipitate (100 mg.) which was recrystallised from aqueous ethanol to give pale-yellow prisms, m. p. 232° (decomp.) (Found: C, 47·7; H, 3·0; O, 31·9; Cl, 17·6; OMe, 6·4%; equiv., 208. Calc. for $C_{16}H_{12}O_6Cl_2$: C, 47·6; H, 3·0; O, 31·8; Cl, 17·6; 1OMe, 7·7%; equiv. for dibasic acid, 202). Erdin hydrate prepared from erdin [1d] which had been isolated from the culture fluid of *Aspergillus terreus* Thom (Ac.45) caused no depression of m. p. on admixture with this product. The compounds had identical infrared spectra and gave the same methylation product, m. p. 121°, on treatment with sodium hydroxide solution and dimethyl sulphate.

(b) *With sulphuric acid.* Dihydrogeodoxin (94 mg.) was suspended in 80% sulphuric acid (5 c.c.) and heated slowly to 125°. During 5 min. at this temperature the solution darkened and effervesced. It was cooled rapidly and diluted with water (15 c.c.), yielding a green precipitate (60 mg.) which was purified by washing with sodium hydrogen carbonate solution to remove tar. The major constituent (20 mg.) was obtained from the neutral residue by crystallisation from chloroform–acetone, and from ethanol, as yellow needles, m. p. 317—319° (decomp.) (Found: C, 53·2; H, 3·0; O, 23·7; Cl, 21·2; OMe, 9·8. $C_{15}H_{10}O_5Cl_2$ requires C, 52·8; H, 2·9; O, 23·5; Cl, 20·8, 1OMe, 9·1%). The ultraviolet and infrared spectra are in agreement with the formulation of this compound as *5,7-dichloro-2-hydroxy-4-methoxy-6-methylxanthone*, $\lambda_{max.}$ 242 (shoulder), 270, 295 (shoulder), 330, 402 mμ (log ε, 3·8, 4·2, 3·3, 3·1, 3·3); the infrared spectrum includes bands at 1640, 1610 (CO), and 1590 cm.$^{-1}$ (aromatic C=C); cf. xanthone,[2] $\lambda_{max.}$ 243, 263, 288, 333 mμ (log ε 4·6, 4·3, 3·7, 3·8) as well as infrared bands at 1660, 1610, and 1585 cm.$^{-1}$ (chloroform solution).

In a second experiment with similar quantities, the green precipitate was dried and sublimed (110°/0·1 mm.) to give a white sublimate (6 mg.), m. p. and mixed m. p. with *methyl 2,5-dihydroxy-3-methoxybenzoate*, 163—166°. The authentic compound was prepared from the corresponding acid [9] by esterification with dimethyl sulphate and sodium hydrogen carbonate in acetone (Found: C, 54·6; H, 5·1; OMe, 32·3. $C_9H_{10}O_5$ requires C, 54·5; H, 5·1; 2OMe, 31·3%). The products obtained by synthesis and degradation gave identical infrared spectra.

The aqueous solution which remained after removal of the green precipitate was extracted with ether which gave, on evaporation, tarry acid (25 mg.). Sublimation (80°/0·1 mm.) led to the separation of the major constituent, m. p. 170°, which was identified as 2,4-dichloro-orcinol by mixed m. p. determination and comparison of the infrared spectrum with that of authentic material.

Department of Chemistry, University College of Swansea.
University College of the West Indies, Jamaica. [*Received, March 20th*, 1959.]

[9] Schock and Tabern, *J. Org. Chem.*, 1951, **16**, 1772.

569. *Triethylenediphosphine* (1 : 4-*Diphospha*bicyclo[2 : 2 : 2]-*octane*).

By Roy C. Hinton and Frederick G. Mann.

Triethylenediphosphine has been synthesised by combining tribenzylphosphine and ethylene dibromide to give the salt

$$[(PhCH_2)_3P{\cdot}C_2H_4{\cdot}P(CH_2Ph)_3]Br_2,$$

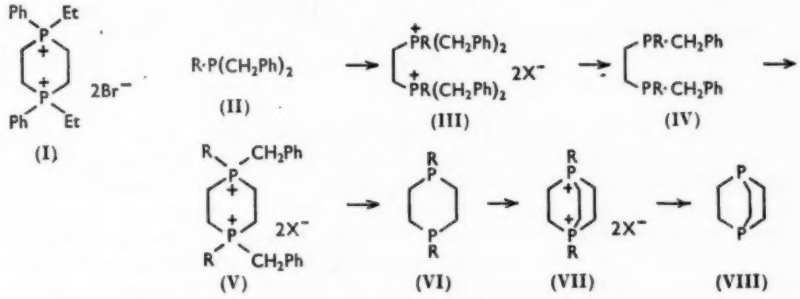
which on treatment with lithium aluminium hydride gives the diphosphine, $(PhCH_2)_3P{\cdot}C_2H_4{\cdot}P(CH_2Ph)_3$. Successive reaction with ethylene dibromide and the hydride give in turn the diphosphine $PhCH_2{\cdot}P<[CH_2{\cdot}CH_2]_2>P{\cdot}CH_2Ph$ and then the triethylenediphosphine.

Triethylenediphosphine, like triethylenediamine, is a highly crystalline, readily volatile substance. The phosphine and certain derivatives show a strong tendency to retain traces of solvent even after sublimation at low pressures.

The action of the lithium aluminium hydride in the last stage of the synthesis also causes a cleavage of the triethylenediphosphine system with the production of a polythene $Me{\cdot}[CH_2]_n{\cdot}Me$, where $n = ca.$ 34.

Two syntheses of 1 : 4-diethyl-1 : 4-diphenyldiethylenediphosphonium dibromide (I), systematically named 1 : 4-diethyl-1 : 4-diphenyl-1 : 4-diphosphonia*cyclo*hexane dibromide, have been recorded by Hitchcock and Mann.[1] The corresponding ditertiary phosphine (VI; R = Ph), which was required for further cyclic diquaternisation with ethylene dibromide, could not be obtained from the salt (I) by thermal decomposition, which caused fission of the ring with formation of *sym*-ethylenebis(ethylphenylphosphine).

Bailey and Buckler[2] have shown, however, that quaternary phosphonium halides having a benzyl group as part of the phosphonium cation lose this group on treatment with lithium aluminium hydride, with liberation of the corresponding tertiary phosphine. We have therefore investigated the application of this reaction to our diphosphonium derivatives, with the ultimate object of isolating triethylenediphosphine (VIII), systematically named 1 : 4-diphospha*bicyclo*[2 : 2 : 2]octane.



In preliminary experiments, dibenzylphenylphosphine[3] (II; R = Ph) was quaternised with ethylene dibromide to form *sym*-ethylenebis(dibenzylphenylphosphonium) dibromide (III; R = Ph, X = Br). This salt, when heated, decomposed with the formation of dibenzylphenylphosphine hydrobromide. When, however, the salt (III; R = Ph; X = Br) in tetrahydrofuran was treated with lithium aluminium hydride, smooth conversion into *sym*-ethylenebis(benzylphenylphosphine) (IV; R = Ph) in 95% yield occurred.

[1] Hitchcock and Mann, *J.*, 1958, 2081.
[2] Bailey and Buckler, *J. Amer. Chem. Soc.*, 1957, **79**, 3567.
[3] Mann, Millar, and Stewart, *J.*, 1954, 2832.

XUM

This diphosphine was characterised by formation of its dimethiodide and its chelated palladobromide derivative (IX; R = Ph).

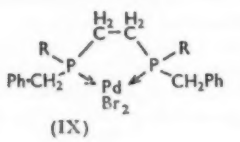
In an attempted alternative synthesis of the diphosphine, a solution of phenylphosphine in liquid ammonia was treated in turn with one equivalent of sodium, benzyl bromide, and sodium again, and finally with half an equivalent of ethylene dibromide (cf. ref. 1). The major product was, however, dibenzylphenylphosphine, with a lower-boiling fraction which was probably benzylphenylphosphine; the diphosphine was not detected.

The diphosphine (IV; R = Ph) reacted vigorously with ethylene dibromide to form the cyclic diphosphonium dibromide (V; R = Ph, X = Br), which on treatment with the hydride as before afforded 1 : 4-diphenyldiethylenediphosphine (VI; R = Ph). The identity of this diphosphine, *i.e.*, the fact that it was not the corresponding derivative having the tetraethylenetetraphosphine ring system, was confirmed by the determination of the molecular weight of its dioxide.

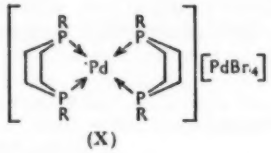
This diphosphine also reacted vigorously with ethylene dibromide to form the bicyclodiphosphonium dibromide (VII; R = Ph, X = Br), but this salt and the corresponding dipicrate were difficult to purify.

This preparation of the dibromide (VII; R = Ph, X = Br) revealed the synthetic route to the dicyclic diphosphine (VIII). For this purpose, tribenzylphosphine (II; R = CH_2Ph) was quaternised with ethylene dibromide to the diphosphonium dibromide (III; R = CH_2Ph, X = Br), which was reduced to the diphosphine (IV; R = CH_2Ph). This diphosphine also readily gave a chelated palladium derivative (IX; R = CH_2Ph).

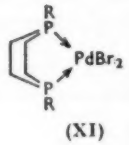
The diphosphine (IV; R = CH_2Ph) in turn gave the cyclic diphosphonium dibromide (V; R = CH_2Ph, X = Br), which on reduction afforded the cyclic diphosphine (VI; R = CH_2Ph). It is noteworthy that cold benzyl bromide reconverted this diphosphine into the cyclic dibromide (V; R = CH_2Ph, X = Br), but boiling benzyl bromide caused ring fission and formation of the original dibromide (III; R = CH_2Ph, X = Br). The diphosphine reacted readily with ethylene dibromide to give 1 : 4-dibenzyltriethylenediphosphonium dibromide (VII; R = CH_2Ph, X = Br).



(IX)



(X)



(XI)

The formation of the triethylenediphosphonium salts (VII; R = Ph and CH_2Ph, X = Br) by the action of ethylene dibromide on the monocyclic diphosphines (VI; R = Ph and CH_2Ph) shows clearly that the ring system in the latter compounds must be capable of existing in the " boat " conformation. This is confirmed by the reaction of potassium palladobromide with warm ethanolic 1 : 4-dibenzyldiethylenediphosphine (VI; R = CH_2Ph) to give the salt (X; R = CH_2Ph), a buff-coloured microcrystalline powder, insoluble in all the usual hot solvents, and the deep orange-brown 1 : 4-dibenzyldiethylenediphosphinedibromopalladium (XI; R = CH_2Ph), which is readily soluble in various solvents and shows a normal molecular weight in boiling chloroform. It is noteworthy that the salt (X; R = CH_2Ph) decomposed without melting between 200° and 300°, whereas the compound (XI; R = CH_2Ph) had m. p. 145—152°. The diphenyldiphosphine (VI; R = Ph) gave an analogous salt (X; R = Ph), having properties almost identical with those of its benzyl homologue: it also gave a soluble orange-brown compound, undoubtedly of type (XI), but insufficient material precluded complete purification.

This behaviour recalls that of *o*-phenylenebisdimethylarsine,[4] $C_6H_4(AsMe_2)_2$, and

[4] Chatt and Mann, *J.*, 1939, 1622.

o-dimethylaminophenyldiethylphosphine,[5] $NMe_2 \cdot C_6H_4 \cdot PEt_2$, each of which reacts readily with potassium palladochloride to give stable insoluble salts of type (X), which on prolonged digestion with boiling ethanolic hydrochloric acid and ethanol respectively undergo conversion into the covalent dichlorides of type (XI).

The 1 : 4-dibenzyldiethylenediphosphinedibromo-palladium (XI; $R = CH_2Ph$) is identical in type with, and closely similar in appearance to, 1 : 4-dimethylpiperazine-dibromopalladium, in which the piperazine ring has also adopted the "boat" conformation.[6]

The reduction of the 1 : 4-dibenzyltriethylenediphosphonium dibromide (VII; $R = CH_2Ph$, $X = Br$) in tetrahydrofuran was carried out as usual with lithium aluminium hydride, the solvent being then removed, and the cold residue treated with ether and aqueous sodium potassium tartrate. Investigation of the ethereal layer showed, however, that the hydride had not only reduced the dibromide to the required triethylenediphosphine (VIII), but had caused considerable rupture of the ring system with the production of (*a*) a polythene $Me \cdot [CH_2]_n \cdot Me$, where $n = ca.\ 34$, formed by polymerisation of the liberated $\cdot CH_2 \cdot CH_2 \cdot$ units, and (*b*) a second phosphine which has not yet been identified.

The ether was removed from the extract, and the distillation apparatus then fitted with an ice-cooled receiver, and heated on a steam-bath whilst nitrogen was passed through the apparatus. The diphosphine (VIII) separated as needle-shaped crystals in the trap.

The pure diphosphine had m. p. 252° under nitrogen in a sealed tube, and showed a normal molecular weight in boiling chloroform solution. It was characterised as its crystalline dimethiodide (XII; $X = I$), dimethopicrate (XII; $X = O \cdot C_6H_2O_6N_3$), and its bis(aurous chloride) derivative (XIII). It sublimes very readily at low pressures, and in this respect resembles triethylenediamine[7] and quinuclidine.[8]

(XII) $Me \cdot {}^{+}P\langle [CH_2 \cdot CH_2]_3 \rangle P^{+}Me, 2X^{-}$ $\qquad$ $ClAu \leftarrow P\langle [CH_2 \cdot CH_2]_3 \rangle P \rightarrow AuCl$ (XIII)

(XIV) $OP\langle [CH_2 \cdot CH_2]_3 \rangle PO$ $\qquad$ $[C_6H_{12}P^{+}]X^{-}$ (XV)

The diphosphine (VIII) and certain derivatives have a remarkable capacity for tenaciously retaining traces of solvent. Distillation of a benzene solution of the diphosphine under nitrogen at 15 mm. gave a crystalline residue, which when sublimed at 100°/0·2 mm. gave crystals of composition $C_6H_{12}P_2,\frac{1}{6}C_6H_6$, and repeated sublimation was necessary to obtain the pure diphosphine. Similarly a very crude sample of the aurous chloride derivative (XIII), prepared directly from the initial ethereal extract, when heated at 300°/0·2 mm., gave a sublimate of composition $C_6H_{12}P_2,\frac{1}{4}H_2O$ in two independent experiments, and this sublimate had the chemical properties of the pure diphosphine. Since it is highly unlikely that the diphosphine and the solvent molecules remained associated in the vapour phase during sublimation, the proportion of solvent in these sublimates is probably fortuitous. These sublimations were carried out in tubes which, being sealed at one end, would never become entirely free from solvent molecules during the sublimation. The passage of a very fine stream of nitrogen through the sublimation tube would probably have accelerated the complete removal of solvent, but would also have caused considerable loss of the volatile diphosphine.

In benzene solution the diphosphine is remarkably protected from oxidation, and it is unaffected when the cold solution is subjected to the passage of a fine stream of oxygen for several hours, or when the hot solution is similarly treated with air, or when the warm solution is treated with acetone–hydrogen peroxide. In cold ethanolic solution, however, the diphosphine is rapidly converted into the crystalline dioxide (XIV), which even after being heated at 150°/1 mm. for five hours had the composition $C_6H_{12}O_2P_2,\frac{1}{3}C_2H_5 \cdot OH$; heating at 220°/1 mm. for 4 hours was necessary to obtain the solvent-free dioxide.

[5] Mann and Watson, *J.*, 1957, 3950.
[6] *Idem*, *J.*, 1958, 2772.
[7] Mann and Baker, *J.*, 1957, 1881.
[8] Meisenheimer, *Annalen*, 1920, **420**, 194.

XUM

Similarly the diphosphine in boiling benzene solution reacted readily with sulphur to give the insoluble disulphide, which however after 4 hr. at 125°/1 mm. had, in two independent experiments, the composition $C_6H_{12}S_2P_2,\frac{1}{8}C_6H_6$. The dibenzyl dibromide (VII; R = CH_2Ph, X = Br) formed a stable hemihydrate, and the corresponding dipicrate a diethanolate.

The non-volatile residue from the initial volatilisation of the diphosphine was extracted with boiling ethanol, leaving an insoluble gum. The ethanol extract deposited white crystalline flakes having a greasy consistency: purification by recrystallisation and then sublimation afforded a hydrocarbon of analytical composition $[CH_2]_n$, and having the molecular weight of 520 in boiling chloroform, and 510 in chloroform at 30°, the latter being determined by the extra-sensitive Thermistor technique.[9] The infrared spectrum of this hydrocarbon was identical with that of a pure sample of the hydrocarbon Me·$[CH_2]_{98}$·Me,[10] kindly supplied by Dr. N. Sheppard, except that the band at 1378 cm.$^{-1}$ due to the methyl groups was about three times as strong in the spectrum of our hydrocarbon as that in the standard compound. It is clear therefore that our hydrocarbon is a polythene of formula Me·$[CH_2]_n$·Me, where n is *ca.* 34.

In an attempt to identify the third constituent of the reduction product, the crude ethereal solvent was added to ethereal methyl iodide, giving an immediate precipitate, which contained traces of aluminium and could not be purified: this iodide was clearly different from the dimethiodide (XII; X = I). The corresponding methobromide and methotoluene-*p*-sulphonate were also prepared. These impure salts all gave the same picrate, of composition (XV; X = $C_6H_2O_7N_3$), which was then converted into the bromide (XV; X = Br) and iodide. The small quantity available of these salts precluded identification, and in the absence of molecular-weight determinations their complexity is unknown. The fact that the quaternised cation contains an even number of carbon atoms may indicate that the salts have been formed from a secondary phosphine which has undergone rapid methylation to the tertiary phosphine before quaternisation.

The infrared spectra of certain of our cyclic diphosphine compounds have been recorded. The spectrum of the diphosphine (VIII) is very simple, in accordance with its symmetrical structure, but shows two sharp bands at 643 and 700 cm.$^{-1}$ associated with the C–P stretching frequency in a tertiary phosphine. The spectrum of the dioxide (XIV) shows the expected strong rather broad band at 1165 cm.$^{-1}$ of the $\geqslant$P=O group. 1 : 4-Dibenzyldiethylenediphosphine monoxide shows bands associated with all these units, namely, the C–P (tertiary phosphine) band at 637, the strong $\geqslant$P=O band at 1165, and the strong sharp C–P=O band at 743 cm.$^{-1}$ Tribenzylphosphine oxide shows the $\geqslant$P=O band at 1188, and the C–P=O band as probably one of two twin bands at 762 and 768 cm.$^{-1}$ respectively, the other being associated with the benzene rings. For comparison, in trimethylphosphine the C–P stretching frequencies appear as two bands at 653 and 708,[11] and in trimethylphosphine oxide the C–P=O frequency gives a strong band at 756, and the $\geqslant$P=O frequency a band at 1170 cm.$^{-1}$.[12]

Experimental

All compounds were colourless unless otherwise stated. To obtain consistent m. p.s, certain compounds were heated in evacuated tubes (noted as E.T.), with the immersion temperature noted as I.T.

Dibenzylphenylphosphine (II; R = Ph) was prepared from dichlorophenylphosphine by the method of Mann, Millar, and Stewart.[3]

sym-*Ethylenebis(dibenzylphenylphosphonium) Dibromide* (III; R = Ph, X = Br).—A mixture of the phosphine (II; R = Ph) (102 g.) and ethylene dibromide (44 g., 0·75 mol.) was heated in nitrogen under reflux on a steam-bath. After *ca.* 1 hr. a vigorous reaction occurred,

[9] Iyengar, *Rec. Trav. chim.*, 1954, **73**, 789.
[10] G. Ställberg, S. Ställberg-Stenhagen, and E. Stenhagen, *Acta Chem. Scand.*, 1952, **6**, 313.
[11] Daasch and Smith, *J. Chem. Phys.*, 1951, **19**, 22.
[12] Rosenbaum, Rubin, and Sandberg, *ibid.*, 1940, **8**, 366.

and was moderated by cooling: the heating was then continued for 2 hr. more. The cool product, on thorough stirring with ether, formed a white solid (119 g., 89%), which when collected, washed with ether, and dried was sufficiently pure for the next stage. The pure *dibromide*, isolated by ethereal precipitation from cold methanolic solution, had m. p. 300—304° (decomp.) (Found: C, 65·1; H, 5·8. $C_{42}H_{42}Br_2P_2$ requires C, 65·6; H, 5·5%). The *dipicrate* (III; R = Ph, X = $C_6H_2O_7N_3$), precipitated from a methanolic solution of the dibromide by sodium picrate, formed yellow crystals, m. p. 209—217° (decomp.), from acetone (Found: C, 61·1; H, 4·2; N, 8·0. $C_{54}H_{46}O_{14}N_6P_2$ requires C, 60·9; H, 4·35; N, 7·9%).

Thermal Decomposition.—The dibromide, when heated in a sublimation tube to *ca.* 270°/0·1 mm., deposited crystals of *dibenzylphenylphosphine hydrobromide*, m. p. 164—166° after resublimation (Found: C, 64·6; H, 5·3. $C_{20}H_{19}P,HBr$ requires C, 64·7; H, 5·4%). A warm ethanolic solution of the hydrobromide, when treated with aqueous-ethanolic potassium palladobromide, deposited the bis(dibenzylphenylphosphine)dibromopalladium, pale yellow crystals (from dioxan), m. p. 244° (decomp.) [lit.,[3] 240—242° (decomp.)] (Found: C, 56·3; H, 4·15. Calc. for $C_{40}H_{38}Br_2P_2Pd$: C, 56·7; H, 4·5%).

sym-*Ethylenebis(benzylphenylphosphine)* (IV; R = Ph).—Lithium aluminium hydride (2 g.) was added under nitrogen to a suspension of the dibromide (III; R = Ph, X = Br) (20 g.) in pure tetrahydrofuran (100 c.c.), which was boiled under reflux for 6 hr., concentrated to *ca.* 15 c.c., and cooled. Undried ether (150 c.c.) was cautiously added, and the hydrolysis completed by slow addition of 20% aqueous sodium potassium tartrate. The ethereal layer was syphoned off under nitrogen pressure, dried (Na_2SO_4), filtered, and distilled, leaving the crude crystalline *diphosphine* (IV; R = Ph) (10·5 g., 95%): a sample, when sublimed at 200°/0·0005 mm., had m. p. 85—98° (E.T.) (Found: C, 78·8; H, 6·95. $C_{28}H_{28}P_2$ requires C, 78·8; H, 6·6%). The crystalline *dimethiodide*, readily formed in hot methyl iodide, had m. p. 300—303° (E.T., I.T. 290°) after crystallisation from methanol (Found: C, 51·1; H, 4·9. $C_{30}H_{34}I_2P_2$ requires C, 50·75; H, 4·8%).

Potassium palladobromide, dissolved in a minimum of water and then diluted with ethanol, was added dropwise to a hot ethanolic solution of the diphosphine until the liquid just became brown. The solution, when boiled, filtered, and cooled, deposited sym-*ethylenebis(benzylphenylphosphine)dibromopalladium* (IX; R = Ph), yellow crystals which, immersed at 200°, slowly became black and melted sharply at 222° (E.T.) (Found: C, 48·8; H, 3·9. $C_{28}H_{28}Br_2P_2Pd$ requires C, 48·5; H, 4·1%).

For the detailed experimental conditions employed in the following preparation, see ref. 1. Sodium (6·4 g., 0·9 equiv.) was added in small pieces to a solution of phenylphosphine (34 g.) in liquid ammonia (300 c.c.). After 15 min., benzyl bromide (44·2 g., 1 mol.) was added dropwise, and then sodium (7·1 g.) as before. The solution was stirred for 1 hr., and then ethylene dibromide (29·1 g., 0·5 mol.) added dropwise with stirring. Finally ether (300 c.c.) was added, followed, after evaporation of the ammonia, by cold freshly boiled water (100 c.c.). The ethereal layer, when syphoned off under nitrogen pressure, dried (Na_2SO_4), and distilled, finally at 0·5 mm., gave fractions: (*a*) b. p. 108—110°, 4·7 g.; (*b*) 110—195°, 1·8 g.; (*c*) b. p. 195—214°, 10·3 g. Fraction (*a*), a foul-smelling, readily oxidised liquid, was probably benzylphenylphosphine. Fraction (*c*) was dibenzylphenylphosphine (12%) (Found: C, 82·8; H, 6·1. Calc. for $C_{20}H_{19}P$: C, 82·7; H, 6·6%). For further characterisation, a portion was converted by hot ethereal benzyl bromide into tribenzylphenylphosphonium bromide, which tended to dissociate on recrystallisation from ethanol and was therefore converted in turn into the yellow *picrate*, m. p. 164·5—166·5° (from ethanolic acetone) (Found: C, 65·0; H, 4·5; N, 6·9. $C_{33}H_{28}O_7N_3P$ requires C, 65·0; H, 4·6; N, 6·9%). A second portion was converted into the pale yellow bis(dibenzylphenylphosphine)dibromopalladium, m. p. 240° (decomp.), 246—247° (decomp.) (E.T.) (from dioxan) (Found: C, 56·6; H, 4·8%).

1 : 4-*Dibenzyl*-1 : 4-*diphenyldiethylenediphosphonium Dibromide* (V; R = Ph, X = Br).—A mixture of the diphosphine (IV; R = Ph) (4 g.) and ethylene dibromide (2·2 g., 1·25 mols.) was heated under nitrogen in a sealed tube at 100° for 6 hr. The product, when thoroughly stirred with ether, collected, and washed with ethanol, afforded the pure *dibromide* (5 g.), m. p. 375° (effervescence, with darkening at 370°) (E.T., I.T. 360°) (Found: C, 58·2; H, 5·7. $C_{30}H_{32}Br_2P_2$ requires C, 58·6; H, 5·25%). The dibromide when treated with sodium picrate, each in aqueous solution, deposited the yellow *dipicrate*, which was too insoluble for recrystallisation and decomposed slowly when heated below 100° (Found: C, 55·6; H, 4·2; N, 9·5. $C_{42}H_{36}O_{14}N_6P_2$ requires C, 55·4; H, 4·0; N, 9·2%).

For the preparation of this dibromide on a larger scale, the isolation of the pure diphosphine (IV; R = Ph) is unnecessary. A suspension of the dibromide (III; R = Ph, X = Br) (120 g.) in tetrahydrofuran (500 c.c.) was treated with lithium aluminium hydride (12 g.) as above, and the ether removed from the dried ethereal extract. Ethylene dibromide (26·4 g.) was added under nitrogen to the crude residual diphosphine, which was then heated on the steam-bath. A vigorous reaction occurred after *ca.* 1 hr., and more dibromide (12 g.) was subsequently added and the heating continued for 1 hr. more. The cold residue when thoroughly triturated with ethanol afforded the pure dibromide (V; R = Ph, X = Br) (32·8 g., 32% overall yield from the dichlorophenylphosphine initially employed).

1 : 4-*Diphenyldiethylenediphosphine* (VI; R = Ph).—The dibromide (V; R = Ph, X = Br) (32·8 g.) in tetrahydrofuran (250 c.c.) was treated as above with the hydride (4·5 g.). Evaporation of the ethereal extract gave the crude *diphosphine* (VI; R = Ph) (7 g.): a sample, twice sublimed at 140°/0·001 mm. and then washed with methanol to remove a liquid impurity (possibly a hydrocarbon), had m. p. 92—95° (E.T.) (Found: C, 70·7; H, 6·7. $C_{16}H_{18}P_2$ requires C, 70·6; H, 6·7%).

When air was passed through a cold ethereal solution of the diphosphine for 4 hr., the *dioxide* separated as a sticky solid, which when digested with boiling acetone formed a fine powder, m. p. 250° (E.T.), 267° (effervescence, E.T., I.T. 220°), in each case with earlier darkening (Found: C, 63·5; H, 5·8%; *M*, in boiling 0·403% chloroform solution, 295. $C_{16}H_{18}O_2P_2$ requires C, 63·2; H, 6·0%; *M*, 304). It is insoluble in most of the usual liquids.

1 : 4-*Diphenyltriethylenediphosphonium Dipicrate* (VII; R = Ph, X = $C_6H_2O_7N_3$).—A mixture of the diphosphine (VI; R = Ph) (1·3 g.) and ethylene dibromide (0·7 g., 1 mol.), when heated in nitrogen under reflux on a water-bath, rapidly underwent a vigorous reaction. After 15 min. the product, when cooled and stirred with ether, became crystalline, but when collected and exposed to air readily became very sticky. Its solution in methanol was therefore treated with methanolic sodium picrate, the orange dipicrate (VII; R = Ph, X = $C_6H_2O_7N_3$), m. p. 240° (effervescence, preliminary darkening) (E.T.), being precipitated (Found: C, 48·2; H, 4·2. Calc. for $C_{30}H_{26}O_{14}N_6P_2$: C, 47·6; H, 3·5%). The dipicrate when warmed with solvents readily gave an almost insoluble gum, and recrystallisation was not achieved.

Bis-(1 : 4-*diphenyldiethylenediphosphine*)*palladium Palladobromide* (X; R = Ph).—This was prepared by the interaction of the diphosphine (0·0469 g.) and potassium palladobromide (0·0790 g.) (0·91 mol.), precisely as the 1 : 4-dibenzyl analogue described below, and obtained as an insoluble dark buff-coloured powder, which after drying at 65°/0·1 mm. for 4 hr. blackened between 290° and 340° with formation of a white sublimate (E.T.) (Found: C, 35·3; H, 3·2. $C_{32}H_{36}Br_4P_4Pd_2$ requires C, 35·7; H, 3·4%).

Tribenzylphosphine (II; R = CH_2Ph).—This phosphine was prepared by a modification of the method of Bailey and Buckler,[3] who however converted the phosphine without isolation into its methobromide. A solution of benzylmagnesium chloride was prepared by the addition of benzyl chloride (200 g.) to a stirred suspension of magnesium (40 g., 1·05 equiv.) in ether (1 l.) at a rate sufficient to maintain gentle boiling under reflux. The mixture was then boiled for 1 hr., cooled, stirred, and treated in turn with benzene (250 c.c.) and dropwise with phosphorus trichloride (65 g.) in benzene (100 c.c.) under nitrogen. The mixture, containing a white deposit, was boiled under reflux for 30 min. and then cooled in ice-water whilst cautiously treated with saturated aqueous ammonium chloride solution (500 c.c.). The ethereal layer was syphoned off under nitrogen pressure and dried (Na_2SO_4), and the solvent removed, leaving the *phosphine* (II; R = CH_2Ph) (122 g., 85%) sufficiently pure for the next stage. It had b. p. 203—210°/0·5 mm., and when twice sublimed at 140°/0·001 mm., had m. p. 92—95° (E.T.) (Found: C, 82·3; H, 7·3. $C_{21}H_{21}P$ requires C, 82·8; H, 7·0%).

When air was passed through an ethereal solution, the *oxide* readily separated as a crystalline powder, m. p. 209—212° (E.T.) (from acetone) (Found: C, 78·5; H, 6·7. $C_{21}H_{21}OP$ requires C, 78·7; H, 6·6%). The *methiodide*, prepared in the normal way, formed crystals, m. p. 170—171° (E.T.), from ethanol (Found: C, 59·0; H, 5·2. $C_{22}H_{24}IP$ requires C, 59·2; H, 5·4%).

sym-*Ethylenebis*(*tribenzylphosphonium*) *Dibromide* (III; R = CH_2Ph, X = Br).—A mixture of the phosphine (II; R = CH_2Ph) (122 g.) and ethylene dibromide (44 g., 1·2 mols.) was heated in a 250 c.c. flask under reflux on a steam-bath. A vigorous reaction occurred after *ca.* 1 hr.; more ethylene dibromide (22 g.) was added and heating continued for 2 hr. more. The product when thoroughly washed with ether afforded the crude *dibromide* (160 g., 97%) suitable for the next stage: a sample, recrystallised from methanol, had m. p. 275—279° (E.T.)

XUM

(Found: C, 65·9; H, 5·8. $C_{44}H_{46}Br_2P_2$ requires C, 66·3; H, 5·8%). In methanolic solution, it readily deposited the yellow *dipicrate*, m. p. 220—222° (effervescence, previous darkening, E.T) (from ethyl methyl ketone) (Found: C, 61·4; H, 4·8; N, 7·75. $C_{56}H_{50}O_{14}N_6P_2$ requires C, 61·5; H, 4·6; N, 7·7%).

sym-*Ethylenebis(dibenzylphosphine)* (IV; R = CH_2Ph).—This was prepared precisely as the diphosphine (IV; R = Ph), evaporation of the ethereal extract giving the crude product in 76% yield. A sample after sublimation at 180°/0·01 mm. still contained a trace of impurity (Found: C, 80·4; H, 7·1. $C_{30}H_{32}P_2$ requires C, 79·3; H, 7·1%). It gave the *diphosphinedibromopalladium* (IX; R = CH_2Ph), as fine pale brown crystals, m. p. 215—217° (considerable preliminary darkening) (from ethanol) (Found: C, 49·9; H, 4·3. $C_{30}H_{32}Br_2P_2Pd$ requires C, 50·0; H, 4·5%).

1 : 1 : 4 : 4-*Tetrabenzyldiethylenediphosphonium Dibromide* (V; R = CH_2Ph, X = Br).—This salt was prepared in the usual way from the diphosphine (IV; R = CH_2Ph) (25 g.) and two additions of ethylene dibromide (13·2 g., 1 + 0·3 mols.). The crude product on recrystallisation from ethanol gave the *dibromide* (15 g., 37% yield from phosphorus trichloride), m. p. 287—292° (effervescence, E.T.) (Found: C, 59·8; H, 5·8. $C_{32}H_{36}Br_2P_2$ requires C, 59·8; H, 5·6%). It gave a yellow *dipicrate*, m. p. 214° (decomp., E.T.) (Found: N, 8·6. $C_{44}H_{40}O_{14}N_6P_2$ requires N, 8·95%).

1 : 4-*Dibenzyldiethylenediphosphine* (VI; R = CH_2Ph).—The crude *diphosphine* was obtained in 76% yield by the usual reduction: a portion, when recrystallised from ethanol, sublimed at 200°/0·5 mm., washed with ethanol and resublimed, had m. p. 128—130° (under nitrogen in sealed tube) (Found: C, 72·3; H, 7·85. $C_{18}H_{22}P_2$ requires C, 72·0; H, 7·4%).

Benzyl bromide was added to a cold ethanolic solution of the diphosphine, which on agitation deposited the dibromide (V; R = CH_2Ph, X = Br), m. p. and mixed m. p. 288—292° (effervescence, E.T.) after crystallisation from ethanol. A portion of the diphosphine was heated with an excess of benzyl bromide at 100° for ½ hr. Addition of ether precipitated a white gum which was separated and dissolved in hot ethanol: on cooling, the solution deposited the dibromide (III; R = CH_2Ph, X = Br), which was now insoluble in ethanol, but after crystallisation from methanol had m. p. 275—280°, mixed with the authentic salt (III; R = CH_2Ph, X = Br) 278—280°, mixed with the salt (V; R = CH_2Ph, X = Br) 260—263° (all E.T.).

When air was passed through an ethereal solution of the diphosphine, the *monoxide* separated as a gum which was converted into a powder by the addition of acetone and the evaporation of the ether by the air-stream, and when then recrystallised from propan-1-ol had m. p. 302—305° (I.T. 290°) (Found: C, 68·6; H, 7·4%; *M*, in 0·384% boiling chloroform, 293. $C_{18}H_{22}OP_2$ requires C, 68·4; H, 7·0%; *M*, 316). An acetone solution of the monoxide, when treated with hydrogen peroxide, deposited a powder, undoubtedly the dioxide, insoluble in all the normal liquids.

1 : 4-*Dibenzyltriethylenediphosphonium Dibromide* (VII; R = CH_2Ph, X = Br).—A mixture of the diphosphine (VI; R = CH_2Ph) (6·5 g.) and ethylene dibromide (5·5 g., 1·4 mols.), when heated on a steam-bath, underwent a violent reaction. More ethylene dibromide (2 g.) was added and the mixture heated for 30 min., cooled, and washed with cold ethanol. The crude *dibromide* (7 g., 66%) became sticky on exposure to air: a fresh sample, when washed with ethanol, methanol, and ether, and dried at 110°/0·1 mm. for 7 hr., was apparently still a *hemihydrate*, m. p. 340—344° (effervescence, preliminary darkening) (E.T.) (Found: C, 48·6; H, 5·8. $C_{20}H_{26}Br_2P_2,\frac{1}{2}H_2O$ requires C, 48·3; H, 5·5%). It was extremely hygroscopic. A very dilute hot aqueous solution, when treated with aqueous sodium picrate, deposited the yellow *dipicrate*, which when collected and washed with ethanol became orange in colour, apparently with conversion into a *diethanolate*; this was heated at 50°/0·1 mm. for 3 hr. (Found, in independent preparations: C, 49·1, 49·5; H, 5·1, 4·5; N, 9·65, 9·6. $C_{32}H_{30}O_{14}N_6P_2,2C_2H_6O$ requires C, 49·3; H, 4·8; N, 9·6%): on heating (E.T.), the colour became paler from 140°, a yellow sublimate formed from 195° and the black residue melted at 243°.

Palladium Bromide Derivatives of the Diphosphine (VI; R = CH_2Ph).—A solution of potassium palladobromide (0·4704 g., 0·89 mol.) in a minimum of warm water was diluted with hot ethanol (10 c.c.) and then slowly added to a stirred boiling solution of the diphosphine (0·3136 g., 1 mol.) in ethanol (80 c.c.). The colour of the palladobromide was rapidly discharged and a yellow almost amorphous product began to separate, but the final solution was red. The insoluble *bis*-(1 : 4-*dibenzyldiethylenediphosphine)palladium palladobromide* (X; R = CH_2Ph), when collected from the boiling mixture, washed in turn with hot ethanol, water, cold

XUM

ethanol, and ether, and dried at 60°/0·1 mm. for 8 hr., formed a dark buff-coloured powder, which blackened slowly between 200° and 300° with the formation of a white sublimate (E.T.) (Found: C, 38·0; H, 3·8. $C_{36}H_{44}Br_4P_4Pd_2$ requires C, 38·15; H, 3·9%).

The initial filtrate was allowed to evaporate to *ca.* 40 c.c., filtered to remove a small crop of the palladobromide, and then evaporated in a desiccator to dryness. The orange residue was washed with water, dried, and extracted with boiling acetone. The filtered extract on evaporation afforded 1 : 4-*dibenzyldiethylenediphosphine dibromopalladium* (XI; R = CH_2Ph)1 an orange crystalline powder, m. p. 145—152° (preliminary softening) after drying at 55°/0·d mm. for 5 hr. (Found: C, 38·1; H, 3·8%; *M*, in 0·286% chloroform, 524. $C_{18}H_{22}Br_2P_2P$, requires C, 38·15; H, 3·9%; *M*, 567). It is readily soluble in cold ethanol.

Reduction of 1 : 4-*Dibenzyltriethylenediphosphonium Dibromide* (VII; R = CH_2Ph, X = Br).—Lithium aluminium hydride (2 g.) was added under nitrogen to a suspension of the dibromide (4 g.) in tetrahydrofuran (100 c.c.) which was boiled under reflux for 6 hr. The solvent, after being distilled off, did not contain any tertiary phosphine. The cold residue was treated with ether, and then hydrolysed as before. The ether extract was collected under nitrogen, dried, and pumped slowly into a small distilling-flask so that the rates of addition and distillation were almost equal. The distilled ether was also free from tertiary phosphine. The receiver was then replaced by a narrow cylindrical trap in which the entry tube reached almost to the bottom. The trap was immersed in ice-water whilst the residue was heated on the steam-bath, with the nitrogen passing through the apparatus throughout the whole operation. Deposition of the crystalline diphosphine (VIII) in the trap was complete after *ca.* 6 hours' heating. The diphosphine was then dissolved out of the trap with benzene, which was distilled off at 15 mm. The crystalline residue was sublimed in nitrogen at 100°/0·2 mm., giving the impure diphosphine (Found: C, 53·1; H, 8·3. Calc. for $C_6H_{12}P_2,\frac{1}{6}C_6H_6$: C, 52·8; H, 8·2%). Repeated resublimation ultimately gave the pure *diphosphine* (VIII), which when heated in a sealed tube under nitrogen on a Kofler stage had m. p. 252° with partial sublimation (Found: C, 49·4; H, 8·2%; *M*, in 0·260% freezing benzene, 136. $C_6H_{12}P_2$ requires C, 49·3; H, 8·3%; *M*, 146). The true yield of the diphosphine in this preparation is difficult to assess, chiefly because of losses during sublimation, but the pure solvent-free diphosphine isolated weighed 30 mg. The diphosphine is freely soluble in cold methanol, ethanol, ether, and benzene.

When the crude ethereal extract was added to ethereal chloroauric acid ($HAuCl_4,4H_2O$), the latter was reduced, with the precipitation of an impure dark yellow chloroaurous derivative. This product, when collected, washed, dried, and heated at 300°/0·2 mm., gave a crystalline sublimate of the diphosphine (VIII) still associated with water (Found, in independent experiments: C, 48·0, 48·1; H, 8·7, 8·9. Calc. for $C_6H_{12}P_2,\frac{1}{4}H_2O$: C, 47·85; H, 8·4%). This sublimate, when treated cautiously with chloroauric acid, each in ethereal solution, deposited the pure yellow *triethylenediphosphinedichlorodigold* (XIII), which decomposed within 24 hr. at room temperature (Found: C, 11·7; H, 2·3. $C_6H_{12}Cl_2P_2Au_2$ requires C, 11·8; H, 2·0%). The yield of the sublimed diphosphine (VIII) by this method is, however, very small and uncertain.

The following derivatives were prepared from the diphosphine (VIII) obtained by the first method.

The addition of an excess of methyl iodide to a cold methanolic solution of the diphosphine gave no apparent reaction until the mixture was warmed; the *dimethiodide* (XII; X = I), m. p. 375—380° (effervescence) (E.T.), was deposited (Found: C, 22·8; H, 4·3. $C_8H_{18}I_2P_2$ requires C, 22·35; H, 4·2%). It is readily soluble in cold water, but almost insoluble in boiling methanol and ethanol. Its cold aqueous solution, treated with aqueous sodium picrate, deposited the *dimethopicrate* (bright yellow crystals from hot water), m. p. 270° (effervescence, with progressive darkening from 130°) (E.T.), m. p. 278° (effervescence, previous darkening) (E.T., I.T. 240°) (Found: C, 38·0; H, 3·6; N, 13·3. $C_{20}H_{22}O_{14}N_6P_2$ requires C, 38·0; H, 3·5; N, 13·3%). It is very slightly soluble in hot acetone, and insoluble in boiling methanol and ethanol.

A cold ethanolic solution of the diphosphine was exposed to the air for 10 hr. and then evaporated in a desiccator. The residual crystalline *dioxide* (XIV) was heated at 150°/1 mm. for 5 hr. (Found: C, 41·6; H, 7·0. Calc. for $C_6H_{12}O_2P_2,\frac{1}{3}C_2H_6O$: C, 41·4; H, 7·3%), and then at 220°/1 mm. for 4 hr. (Found: C, 40·5; H, 6·6. $C_6H_{12}O_2P_2$ requires C, 40·5; H, 6·8%): on heating (E.T.) it sublimed slowly above 300°. It is freely soluble in cold methanol and ethanol, and very sparingly soluble in other organic solvents.

A benzene solution of the diphosphine, when added to a boiling benzene solution of rhombic sulphur, caused a rapid deposition of the insoluble disulphide, which, however, after being heated at 125°/0·1 mm. for 4 hr., still contained solvent (Found, in independent preparations: C, 36·7, 36·9; H, 5·8, 5·9. Calc. for $C_6H_{12}S_2P_2,\frac{1}{8}C_6H_6$: C, 36·85; H, 5·9%). It decomposed slowly without melting above 400°.

The residue in the flask, after the volatilisation of the diphosphine (VIII) in nitrogen, was extracted with boiling ethanol, which, when filtered to remove an insoluble colourless gum and cooled, deposited white greasy crystals of the hydrocarbon. This was twice recrystallised from ethanol and then sublimed at 300°/0·2 mm. (Found: C, 85·9; H, 14·4%; *M*, in 1·702% chloroform solution at 30°, 510; *M*, in 0·3815% boiling chloroform solution, 520). When heated, it slowly softened and melted below 100°.

A blank experiment, with tetrahydrofuran and the hydride in the absence of the phosphonium bromide, showed that this hydrocarbon did not arise by reductive breakdown of the tetrahydrofuran.

Quaternary salts from the crude ethereal extract. A portion of the undried ethereal extract from the reduction was filtered into an excess of ethereal methyl iodide, giving an immediate precipitate, which when collected, thoroughly washed with hot ethanol, and dried, had m. p. 370° (effervescence, shrinking from 345°) (E.T) (Found: C, 30·25, 29·9, 30·4; H, 4·9, 5·1, 4·7%). It was insoluble in all organic solvents: it dissolved in boiling water but separated on cooling as a thick syrup. The corresponding methobromide was prepared at 0°, and set aside overnight. The mother-liquor was decanted, and the residual gummy deposit, after being hardened by digestion with boiling methanol, had m. p. 400° (effervescence, shrinking from 385°) (E.T.): this methobromide was hygroscopic, and was analysed after exposure to air to constant weight (Found: C, 33·1; H, 5·8%). It was soluble in water, but insoluble in boiling methanol and ethanol.

The methotoluene-*p*-sulphonate was prepared similarly to the iodide, but the ether was evaporated from the reaction mixture, and the residue heated at 100° for 30 min. The sulphonate did not crystallise. The above three salts in aqueous or aqueous-ethanolic solution were added to an excess of aqueous sodium picrate. The precipitated yellow picrates (XV; X = $C_6H_2O_7N_3$) did not recrystallise and, when washed with ethanol and dried, became red on heating and decomposed slowly below 200° (Found, for the picrate obtained from the iodide, bromide, and sulphonate respectively, C, 41·85, 42·6, 42·1; H, 4·1, 4·3, 4·2; N, 12·3, 11·95. Calc. for $C_{12}H_{14}O_7N_3P$: C, 42·0; H, 4·1; N, 12·25%).

The picrate was shaken with hot hydrobromic acid, which was then cooled and repeatedly extracted with ether. The mother-liquor was concentrated in a desiccator, and the bromide, m. p. 380° (effervescence) (E.T.), precipitated by acetone (Found: C, 36·3; H, 6·0; Br, 39·0. Calc. for $C_6H_{12}BrP$: C, 37·0; H, 6·2; Br, 41·0%).

The iodide was precipitated by the addition of saturated aquequs sodium iodide to a cold aqueous solution of the bromide, and, when recrystallised from water, had m. p. 370° (effervescence, preliminary shrinking) (E.T.) (Found: C, 28·5; H, 5·5; I, 49·2. Calc. for $C_6H_{12}IP$: C, 29·8; H, 5·0; I, 52·4. Calc. for $C_6H_{12}IP,H_2O$: C, 27·7; H, 5·4; I, 48·8%).

We are greatly indebted to Dr. N. Sheppard for valuable discussions and for the spectrum of the hydrocarbon Me·$[CH_2]_{98}$·Me, which had been supplied by Dr. E. Stenhagen, and to Imperial Chemical Industries Limited, Dyestuffs Division, for a grant (to R. C. H.).

University Chemical Laboratory, Cambridge. [*Received, March 25th*, 1959.]

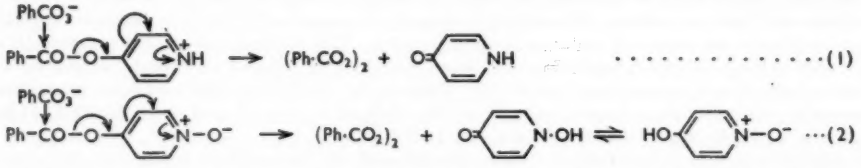
570. *Reactions of Pyridyl Benzoates with Some Perbenzoic Acids.*

By J. I. G. Cadogan.

Whereas 3-pyridyl benzoate with perbenzoic acid in chloroform gives the expected 3-pyridyl benzoate 1-oxide, the 2- and the 4-isomer give dibenzoyl peroxide and no 1-oxide. The mechanisms of the latter and related reactions have been investigated and are discussed.

Although the reactions of peracids with tertiary amines to give the corresponding *N*-oxides are well known for the pyridine series,[1] the reactions of perbenzoic and substituted perbenzoic acids with aromatic esters of the hydroxypyridines have not previously been studied. These reactions were investigated in an attempt to prepare the corresponding *N*-oxides, which were required for another investigation.

When 4-pyridyl benzoate was allowed to react with a large excess of perbenzoic acid in chloroform none of the expected *N*-oxide was isolated or detected, but dibenzoyl peroxide and a mixture of 4-hydroxypyridine and 4-hydroxypyridine 1-oxide were formed. With a slight excess of the peracid, dibenzoyl peroxide and 4-hydroxypyridine 1-oxide appeared; 4-hydroxypyridine was not isolated in this case, but small amounts if present would have been undetected. To account for these products it is considered that the base is first quaternised. This can occur in either or both of two ways: (i) by oxidation of the base to the 1-oxide; (ii) by decomposition of the perbenzoic acid to the stronger benzoic acid, which will protonate the base. Both methods will render the ester liable to nucleophilic attack by perbenzoate anion, as shown. The formation of 4-hydroxypyridine 1-oxide



could in theory arise by direct oxidation of 4-hydroxypyridine produced as in (1), but it has been shown, both in this investigation and elsewhere,[2] that such oxidation does not occur under these conditions. Plainly, the relative extents of reactions (1) and (2) will depend on the experimental conditions, and it was conceivable that conditions could be selected which would give 4-pyridyl benzoate 1-oxide. In an attempt to do this, 4-pyridyl benzoate was treated with less than one equivalent of perbenzoic acid in chloroform. The products were dibenzoyl peroxide, 4-hydroxypyridine, and a trace of an unidentified compound. No oxide was detected. Similar results were obtained from experiments with peranisic acid and 4-pyridyl benzoate. A large excess of the acid gave *p*-anisoyl benzoyl peroxide, 4-hydroxypyridine, and 4-hydroxypyridine 1-oxide. A slight excess of the oxidising agent gave the peroxide and 4-hydroxypyridine, while less than one equivalent of the peracid gave 4-hydroxypyridine 1-oxide, 4-hydroxypyridine, and a trace of the peroxide. In no case was the *N*-oxide of the ester isolated, although traces of unidentified solids were obtained in the last two experiments.

The conclusions summarised in the equations are further supported by the results of the following experiments: 2-pyridyl *p*-nitrobenzoate and perbenzoic acid gave benzoyl *p*-nitrobenzoyl peroxide, and 2-pyridyl benzoate gave benzoyl peroxide.

In each of the above cases the high reactivity of the carbonyl-carbon atom towards nucleophilic substitution is a result of favourable polarisation, induced by the quaternary

[1] Ochiai, *J. Org. Chem.*, 1953, **18**, 534; Katritsky, *Quart. Rev.*, 1956, **10**, 395.
[2] Dr. C. W. Rees, personal communication.

nitrogen atom. Such polarisation can operate only in the 2- and the 4-isomer. If this rationalisation is valid, then the carbonyl-carbon atom in the corresponding 3-isomer should be relatively unreactive towards nucleophilic substitution. This is supported by the isolation of 3-pyridyl benzoate 1-oxide after reactions of perbenzoic acid and of peranisic acid with 3-pyridyl benzoate in chloroform. No diacyl peroxides were isolated or detected.

Experimental

Unless otherwise stated, the light petroleum used had b. p. 60—80°. Perbenzoic and peranisic acid, prepared by standard methods, were stored as approximately 5% solutions in chloroform and were analysed immediately before use.

Preparation of the Isomeric Pyridyl Benzoates.—The hydroxypyridine (1 mol.), as a 10% solution in chloroform, was boiled under reflux for 30 min. with benzoyl chloride (1 mol.). When cool, the solution was washed with potassium carbonate solution and dried ($MgSO_4$). Evaporation of the filtered solution left the pyridyl benzoate. 2-Pyridyl benzoate was distilled (b. p. 136°/0·4 mm.; m. p. 42°; lit.,[3] m. p. 42°). 3-Pyridyl benzoate had m. p. 51—52° (crystals from light petroleum; lit.,[4] m. p. 51°) (Found: C, 72·5; H, 4·7. Calc. for $C_{12}H_9O_2N$: C, 72·3; H, 4·6%). 4-Pyridyl benzoate had m. p. 79—80° (crystals from light petroleum; lit.,[5] m. p. 81°) (Found: C, 72·3; H, 4·6%). 2-Pyridyl *p*-nitrobenzoate (m. p. 120°, crystals from light petroleum; lit.,[3] m. p. 116°) was prepared similarly.

p-Anisoyl benzoyl peroxide (m. p. 73·5°; crystals from light petroleum) (Found: C, 66·4; H, 4·5. Calc. for $C_{15}H_{12}O_5$: C, 66·2; H, 4·4%) was prepared by shaking an ice-cold solution of peranisic acid in chloroform containing the equivalent amount of benzoyl chloride with an excess of ice-cold 2N-potassium hydroxide. Working up the chloroform solution gave the peroxide. Benzoyl *p*-nitrobenzoyl peroxide (m. p. 115—116°; crystals from light petroleum) (Found: C, 58·2; H, 3·2. Calc. for $C_{14}H_8O_6N$: C, 58·5; H, 3·1%) was similarly prepared from perbenzoic acid and *p*-nitrobenzoyl chloride. 4-Hydroxypyridine 1-oxide was prepared as described by Den Hertog and Combe.[6]

Reaction of Perbenzoic Acid with 3-Pyridyl Benzoate.—3-Pyridyl benzoate (5 g.) was added to a 5% solution of perbenzoic acid in chloroform (85 ml.). The mixture was kept at room temperature for 3 days, then washed with sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation left buff crystals (4·5 g.) which, recrystallised from ethyl acetate followed by light petroleum–benzene, gave *3-pyridyl benzoate 1-oxide* as prisms (3·1 g.), m. p. 127° (Found: C, 66·9; H, 4·1. $C_{12}H_9O_3N$ requires C, 67·0; H, 4·2%).

Reaction of Peranisic Acid with 3-Pyridyl Benzoate.—The procedure was essentially as in the preceding paragraph. The product was 3-pyridyl benzoate 1-oxide, m. p. and mixed m. p. 127°.

Reaction of 2-Pyridyl Benzoate with Perbenzoic Acid.—The ester (2 g.) was left at room temperature in a 5% chloroform solution of perbenzoic acid (40 ml.) for 48 hr. Working up as described in the previous experiment gave dibenzoyl peroxide (1·65 g.), m. p. 97—104° (decomp.), mixed m. p. 102—104° (decomp.), and correct infrared spectrum.

Reaction of 2-Pyridyl p-Nitrobenzoate with Perbenzoic Acid.—The ester (0·3 g.) and 5% perbenzoic acid solution (20 ml.) were caused to react as described above. They gave crude benzoyl *p*-nitrobenzoyl peroxide (0·38 g.), m. p. 100—108°, m. p. undepressed on admixture with authentic material. Recrystallisation from light petroleum gave the pure peroxide (0·3 g.), m. p. and mixed m. p. 115°. The aqueous solution was acidified and the benzoic acid was extracted with methylene chloride. The aqueous solution was evaporated almost to dryness, then the pH was adjusted to 7 and evaporation continued to dryness. The residue was extracted with boiling acetone (3 × 50 ml.). Evaporation of the acetone left a buff solid (0·1 g.) which gave a picrate (0·15 g.), m. p. 165—169° (from acetone), m. p. undepressed on admixture with authentic 2-hydroxypyridine picrate (m. p. 169—170°).

Reactions of 4-Pyridyl Benzoate.—(i) *With perbenzoic acid (5 equivalents).* The ester (0·7 g.), with the peracid (5·5%; 45 ml.), was left for 72 hr. at 20°; a gum (0·1 g.) was deposited which proved to be 4-hydroxypyridine 1-oxide (picrate, m. p. and mixed m. p. 165°) admixed with benzoic

[3] Chichibabin and Szokov, *Ber.*, 1925, **58**, 2650.
[4] Cavallito and Haskell, *J. Amer. Chem. Soc.*, 1944, **66**, 1166.
[5] Arndt and Kalischek, *Ber.*, 1930, **63**, 587.
[6] Den Hertog and Combe, *Rec. Trav. chim.*, 1952, **71**, 752.

XUM

acid. The filtered solution was washed with aqueous potassium carbonate and dried ($MgSO_4$). Evaporation of the chloroform solution left dibenzoyl peroxide (0·65 g.), m. p. and mixed m. p. 102° (decomp.). The aqueous portion was acidified and the benzoic acid was extracted with methylene chloride, the aqueous solution was evaporated, and the residue extracted with ethanol. Evaporation of the ethanol left a brown residue which gave a picrate, which on fractional crystallisation from water gave 4-hydroxypyridine picrate (0·28 g.), m. p. and mixed m. p. 235°, and the more soluble 4-hydroxypyridine 1-oxide picrate (0·08 g.), m. p. and mixed m. p. 164°.

In a similar experiment 4-pyridyl benzoate (1·4 g.) was treated with slightly less perbenzoic acid (5%; 70 ml.). In this case 4-hydroxypyridine 1-oxide (0·55 g.; m. p. and mixed m. p. 238—240°) separated as pale yellow crystals, uncontaminated with benzoic acid. The chloroform solution gave dibenzoyl peroxide [1·48 g.; m. p. and mixed m. p. 99—103° (decomp.)].

(ii) *With perbenzoic acid* (1·45 *equivalents*). The ester (0·7 g.) and the acid (5·5%; 13 ml.) were caused to react in the usual way. 4-Hydroxypyridine 1-oxide (0·1 g.; m. p. and mixed m. p. 239—240°) was precipitated. Dibenzoyl peroxide [0·25 g.; m. p. and mixed m. p. 100° (decomp.)] and 4-hydroxypyridine 1-oxide picrate (0·5 g.; m. p. and mixed m. p. 165°) were also isolated.

(iii) *With perbenzoic acid* (0·72 *equivalent*). The ester (1·32 g.) and acid (5·5%; 13 ml.) were allowed to react in the usual way. No solid was precipitated. The chloroform solution was extracted with aqueous potassium carbonate and then with 2N-hydrochloric acid. Evaporation of the chloroform solution left dibenzoyl peroxide [0·18 g.; m. p. and mixed m. p. 104—105° (decomp.)]. Basification and extraction of the acidic washings gave the ester and a trace of an unidentified colourless solid, m. p. 70—105°. Working up the alkaline washings in the usual way gave 4-hydroxypyridine picrate (0·35 g.; m. p. and mixed m. p. 232°).

(iv) *With peranisic acid* (5 *equivalents*). The ester (0·7 g.) was treated with 5·4% peranisic acid solution (55 ml.) in the usual way. The colourless solid (1·95 g.) which was deposited was treated with water and filtered off. The residue (1·6 g.) was *p*-anisic acid, m. p. and mixed m. p. 180°. The filtrate gave 4-hydroxypyridine picrate (0·2 g.), m. p. and mixed m. p. 238°. Concentration of the mother-liquors gave another picrate (0·35 g.; m. p. 140—160°) which, on recrystallisation from water gave 4-hydroxypyridine 1-oxide picrate, m. p. and mixed m. p. 158—161°. The chloroform solution gave yellow *p*-anisoyl benzoyl peroxide (0·6 g.), m. p. 67—72°; recrystallisation from light petroleum gave the pure peroxide.

In a similar experiment involving the ester (1·4 g.) and less peranisic acid in more dilute solution (2%; 100 ml.), 4-hydroxypyridine 1-oxide (0·62 g.; m. p. and mixed m. p. 238—241°) was deposited. Crude anisoyl benzoyl peroxide (1·4 g.), m. p. 64—69° (m. p. and mixed m. p. 71—74° after recrystallisation from light petroleum), was also isolated.

(v) *With peranisic acid* (1·45 *equivalents*). The ester (0·7 g.) with the acid (5·4%; 16 ml.) gave a solid (0·48 g.; m. p. 145°) which was a mixture of *p*-anisic acid and 4-hydroxypyridine 1-oxide (picrate, m. p. and mixed m. p. 161—165°). The chloroform solution on evaporation left a gum which, on extraction with light petroleum, gave colourless crystals (0·1 g.; m. p. 70—90°). Repeated recrystallisation gave a solid, m. p. 114—115°, which could not be identified. Evaporation of the light petroleum mother-liquors left anisoyl benzoyl peroxide (0·2 g.), m. p. and mixed m. p. 69°.

(vi) *With peranisic acid* (0·72 *equivalent*). The ester (0·7 g.) with the acid (5·4%; 8 ml.) deposited no solid. Working up as described in (v) gave a trace of anisoyl benzoyl peroxide, an unidentified solid, m. p. 130—150° (trace), unchanged ester, 4-hydroxypyridine picrate (0·12 g., m. p. and mixed m. p. 235°), and 4-hydroxypyridine 1-oxide picrate (50 mg.; m. p. and mixed m. p. 167—168°).

Reaction of 4-Hydroxypyridine with Perbenzoic Acid.—4-Hydroxypyridine (0·5 g.) and perbenzoic acid in chloroform (5% solution; 40 ml.) were kept at room temperature for 48 hr. No solid had been precipitated in this time and 4-hydroxypyridine was recovered almost quantitatively from the solution as the picrate, m. p. and mixed m. p. 238—239°.

The author is grateful to Professor D. H. Hey, F.R.S., for his advice and interest.

KING'S COLLEGE, STRAND, LONDON, W.C.2. [*Received, April 2nd*, 1959.]

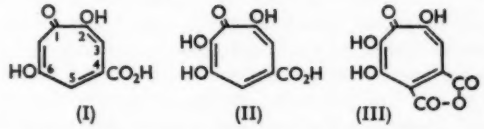
571. *Stipitatonic Acid. A New Mould Tropolone from* Penicillium stipitatum *Thom.**

By W. Segal.

Stipitatonic acid (6-hydroxytropolone-4,5-dicarboxylic acid anhydride) has been isolated from the Czapek–Dox culture fluid of *Penicillium stipitatum*. Its properties and structure are analogous to those of puberulonic acid. Partial decarboxylation of stipitatonic acid produces stipitatic acid. This accumulates in the culture fluid at the expense of the stipitatonic acid.

As a preliminary to the study of the biosynthesis of stipitatic acid, the mould tropolone elaborated by *P. stipitatum*,[1] a method of assaying the metabolite was investigated. As a result a new mould tropolone, stipitatonic acid, has been isolated from the culture fluid.

Reviews [2] have described the chemistry of the three known mould tropolones, namely, stipitatic (I), puberulic (II), and puberulonic acid (III). To date the mould tropolones have been reported as metabolites of the genus *Penicillium* only: puberulic and puberulonic acid from *P. puberulum* Bainier,[3] *P. aurantio-virens* Biourge,[3,4] *P. Johannioli* Zaleski, and *P. cyclopium-viridicatum* series; [5] stipitatic acid from *P. stipitatum* Thom [1] only.



(I) (II) (III)

Stipitatonic acid, $C_9H_4O_6$, was obtained as bright yellow prisms from the culture fluid by concentration under reduced pressure, acidification, and ether-extraction. Stipitatic acid is extracted simultaneously but the new metabolite can be separated by selective sublimation. The composition, colour, and colour reactions of stipitatonic acid suggested its relation to stipitatic acid (I) in the manner [6] of puberulonic (III) to puberulic acid (II). This was confirmed by the quantitative conversion of stipitatonic into stipitatic acid under the conditions reported [7] for converting puberulonic acid into puberulic acid, namely, refluxing in aqueous solution.

Puberulonic acid condenses with *o*-phenylenediamine,[4b] giving a compound, $C_{15}H_8O_5N_2$, which was assigned structure (IV; R = OH) when the anhydride nature of puberulonic acid was established spectroscopically.[6b,8,9] By similar treatment stipitatonic acid gives a refractory vermilion-coloured compound, $C_{15}H_8O_4N_2$, analogous to the puberulonic acid condensation compound. Crow, Haworth, and Jefferies [10] obtained from tropolone-3,4-dicarboxylic anhydride and *o*-phenylenediamine a brown crystalline product which could not be recrystallized; they suggested that it was probably an *N*-*o*-aminophenylimide (V). Stipitatonic acid also produces an intermediate condensation compound (probably $C_{15}H_{10}O_5N_2$) analogous to the compound described by Crow *et al.*[10] Attempts to recrystallize it were unsuccessful and heating it under reflux in a large volume of ethanol

* Briefly reported in part in *Chem. and Ind.*, 1957, 1040; 1958, 1726.

[1] Birkinshaw, Chambers, and Raistrick, *Biochem. J.*, 1942, **36**, 242.

[2] Nozoe, *Fortschr. Chem. org. Naturstoffe*, 1956, **13**, 232; Pauson, *Chem. Rev.*, 1955, **55**, 9; Cook and Loudon, *Quart. Rev.*, 1951, **5**, 99.

[3] Birkinshaw and Raistrick, *Biochem. J.*, 1932, **26**, 441.

[4] (*a*) Barger and Dorrer, *ibid.*, 1934, **28**, 11; (*b*) Corbett, Hassall, Johnson, and Todd, *J.*, 1950, 1.

[5] Oxford, Raistrick, and Smith, *Chem. and Ind.*, 1942, **41**, 485.

[6] (*a*) Aulin-Erdtman and Theorell, *Acta Chem. Scand.*, 1950, **4**, 1490; (*b*) Johnson, Sheppard, and Todd, *J.*, 1951, 1139.

[7] Corbett, Johnson, and Todd, *J.*, 1950, 6.

[8] Aulin-Erdtman, *Acta Chem. Scand.*, 1951, **5**, 301.

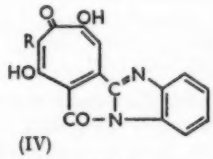
[9] *Idem*, *ibid.*, 1950, **4**, 1325.

[10] Crow, Haworth, and Jefferies, *J.*, 1952, 3705.

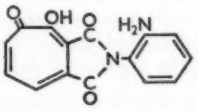
XUM

gave the vermilion-coloured product. This conversion supports the structure (V) suggested by Crow *et al.*

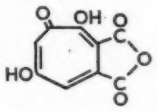
In dioxan the ultraviolet absorption of stipitatonic acid is highly comparable with that of puberulonic acid, the bands for the latter being at somewhat longer wavelengths. Aulin-Erdtman [8] has drawn attention to the unsuitability of water of undefined pH as solvent for measuring the detailed absorption spectra of easily ionizable solutes. It appears that



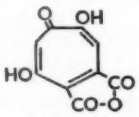
(IV)



(V)



(VI)

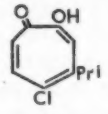


(VII)

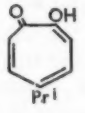
stipitatonic acid is more highly dissociated in water than in dioxan. The spectrum of an aqueous solution (yellow) has a relatively feeble band at 432 mμ. The spectrum of a dioxan solution of comparable concentration (colourless) lacks this band. Addition of water to a colourless dioxan solution produces a marked yellow colour.

The infrared absorption spectrum of stipitatonic acid in " Nujol " mull shows a doublet at 1642 and 1621 cm.$^{-1}$ and a band at 1599 cm.$^{-1}$ [assigned to the tropolone nucleus (cf. doublet at 1639 and 1626 and band at 1577 cm.$^{-1}$ for tropolone-3,4-dicarboxylic anhydride [10])], and intense bands at 1746 and 1824 cm.$^{-1}$ (anhydride); the separations of the anhydride peaks for spectra of puberulonic acid [6b,9] and tropolone-3,4-dicarboxylic anhydride [10] (60 and 45 cm.$^{-1}$ respectively) are somewhat less than for stipitatonic acid.

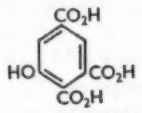
These reactions and properties of stipitatonic acid may be explained by the structures (VI) or (VII). Coupling of tropolones with diazonium salts has been claimed by Pauson [2] as a test for a vacant 5-position in tropolones. An alkaline solution of stipitatonic acid with diazotized *p*-toluidine gave (on acidification) a reddish-brown amorphous solid which, however, was not an azo-compound; attempts to crystallize it produced tars or gums. Stipitatic acid, which possesses a vacant 5-position, gave a similar but paler amorphous solid. In this respect stipitatic and stipitatonic acid are similar to 5-chloro-hinokitiol (VIII) which gives reddish-brown amorphous products with diazonium salts.[11] In addition γ-thujaplicin (IX) affords [12] " red products " on treatment with diazotized amines.



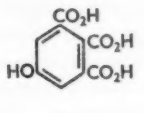
(VIII)



(IX)



(X)



(XI)

The isomerization of tropolones to benzenoid compounds by alkali [2] has on occasions been carried out under very drastic conditions (potassium hydroxide at 300°); though the possibility of migration of groups should not be overlooked, this has not been reported for tropolonoid compounds and potash fusion affords unambiguous preparations of phenol-polycarboxylic acids from the corresponding sulphonated acids. Crow *et al.*[10] reported the isomerization of tropolone-3,4-dicarboxylic anhydride to hemimellitic acid by fusion with sodium hydroxide. Fusion of stipitatonic acid with potassium hydroxide yielded a phenolic acid which on methylation afforded trimethyl 6-methoxybenzene-1,2,4-tricarboxylate.[13] Thus the phenolic acid has structure (X), and stipitatonic acid has structure (VII). The isomeric structure (VI) would be expected to produce the acid (XI), the fully methylated derivative [13] of which melts at 85°, 60° lower than that of the fully methylated acid (X).

[11] Nozoe, Mukai, and Takase, *Proc. Japan Acad.* 1951, **27**, 236.
[12] Erdtman and Gripenberg, *Acta Chem. Scand.*, 1948, **2**, 625.
[13] Gardner, Grove, and Ismay, *J.*, 1954, 1817.

On this basis the *o*-phenylenediamine condensation compound of stipitatonic acid has structure (IV; R = H) or the isomeric structure in which the 5-substituent is bonded to both nitrogen atoms. The intermediate compound is probably the corresponding *N*-*o*-aminophenylimide analogous to (V).

Rate of Production of Stipitatonic Acid.—The concentration of stipitatonic acid in the culture medium reaches a maximum after approximately 25 days; thereafter that of stipitatic acid increases at the expense of the stipitatonic acid. In spite of the instability of stipitatonic acid its conversion into stipitatic acid could be avoided by isolating the metabolites from the samples of acidified culture fluid maintained at room temperature throughout the determination. The quantitative partial decarboxylation and determination of the carbon dioxide produced served as a means of assaying the stipitatonic acid present in the ether-extracted metabolites. Examination of the extracts * by sublimation, fractional crystallization, and paper chromatography failed to detect the presence of more than traces of other components. The results of the determination are summarized in the Table.

Rate of production of stipitatonic acid by P. stipitatum *Thom. growing on Czapek–Dox medium at* 24°.

Incubation period (days)	pH	Residual glucose (%)	Yield of ether-soluble extract (g./l.)	Stipitatonic acid in medium (g./l.)	Stipitatonic acid in extract (%)	Stipitatic acid in extract (by diff.) (%)
8	3·97	4·0	0·108	0·036	33·4	—
13	4·10	3·5	0·308	0·166	54·1	—
25	3·90	2·2	1·138	0·882	77·5	22·5
33	3·81	1·5	1·309	0·535	40·8	59·2
35	3·81	1·5	1·023	0·370	36·1	63·9
39	3·74	1·1	1·233	0·259	21·0	79·0

Experimental

The strain of *Penicillium stipitatum* Thom used (L.S.H.T.M. Cat. No. P 199) has been described by Birkinshaw *et al.*[1] The cultural conditions were those described by them.

Isolation and Purification of Stipitatonic Acid.—After 25 days' growth the filtered Czapek–Dox metabolism solution (35 l.) was concentrated under reduced pressure at 45—50° to about 2·5 l., after which it was cooled to 0° and acidified with sulphuric acid (30% v/v) until the pH was 2·0. It was then exhaustively extracted with ether in a continuous liquid–liquid extractor until the extract issuing became colourless (5—6 days). During the extraction a mixture of stipitatic and stipitatonic acid separated, and after removal of this and drying of the filtrate (Na_2SO_4), the remaining solutes were recovered by removal of the ether at reduced pressure (total yield of crude solids, 15·5 g.). Hot acetone removed most of the stipitatonic acid from the powdered extract. The stipitatic acid simultaneously dissolved was partially precipitated by concentrating the acetone extract. Excessive concentration to remove stipitatic acid caused co-precipitation of stipitatonic acid. The solids in the acetone solution were recovered by evaporation at reduced pressure on the water-bath. Sublimation of the residue in a high vacuum at $<130°$ separated stipitatonic (1·2 g.) from stipitatic acid which sublimed only at 190—200° at the same pressure. The yield of stipitatonic acid here is lower than indicated in the Table, apparently owing to decomposition during the concentration of the metabolite solution. The yellow sublimate was crystallized from acetone and *stipitatonic acid* obtained as bright yellow prisms, m. p. 237—237·5° (decomp.) (Found: C, 52·1; H, 2·2. $C_9H_4O_6$ requires C, 51·9; H, 1·9%), $\lambda_{max.}$ in distilled water 253, 333, 369, 432 mμ (log ε 4·45, 3·81, 3·94, 3·36 respectively), in dioxan 258, 355, 382 mμ (log ε 4·39, 3·98, 3·97 respectively). Stipitatonic acid is readily soluble in cold water producing a deep yellow solution, stable for several days at room temperature. It is insoluble in light petroleum, sparingly soluble in hot chloroform, carbon tetrachloride, and benzene, and slightly soluble in ether and ethyl acetate. Addition

* The extracts after 8 and 13 days' inoculation were gummy and contained intractable components. Subsequent extracts possessed the properties of a mixture of stipitatic and stipitatonic acid.

XUM

of sodium hydrogen carbonate solution to an aqueous solution of the acid produces a deepening of the colour which fades slowly. Acidification of the colourless solution partially restores the original yellow colour. Aqueous neutral ferric chloride produces a light-brown stable colour with aqueous solutions of the acid. The solid acid is very slowly soluble in concentrated sulphuric acid with no marked colour change.

Conversion into Stipitatic Acid.—Stipitatonic acid (71·0 mg.) in air-free distilled water (10 ml.) was heated for 8 hr. under reflux while nitrogen (free from carbon dioxide and oxygen) was passed through the solution and bubbled through two cells of standard barium hydroxide solution (10·00 and 5·00 ml.). Carbon dioxide was evolved after a few minutes and the solution became progressively paler during the heating. On cooling, cream-coloured needles separated and the hydrolysis product was collected at 0° and dried to constant weight (59·3 mg.). Evaporation of the filtrate on the water-bath at reduced pressure afforded a cream-coloured solid (3·5 mg.) (total yield, 62·8 mg.; the process $C_9H_4O_6 + H_2O \longrightarrow C_8H_6O_5 + CO_2$ requires 62·1 mg.). Back-titration of the barium hydroxide solution with standard hydrochloric acid indicated that $3{\cdot}45 \times 10^{-4}$ mole of carbon dioxide was produced (theory. $3{\cdot}41 \times 10^{-4}$ mole). After sublimation *in vacuo* at 190°, the hydrolysis product had m. p. 302—304° (decomp.), undepressed on admixture with stipitatic acid. Colour reactions with ferric chloride, sodium hydroxide, and concentrated sulphuric acid were identical with those of stipitatic acid, and the ultraviolet absorption spectrum was identical with that of this acid. Acetylation (sodium acetate as catalyst) gave diacetylstipitatic acid of m. p. 172° (decomp.), identical (mixed m. p.) with a specimen prepared as described by Birkinshaw *et al.*[1]

Condensation Compounds of Stipitatonic Acid with o-Phenylenediamine.—*o*-Phenylenediamine (60 mg.) and stipitatonic acid (107 mg.) in ethanol (15 ml.) were heated on the water-bath for 3·5 hr. Brown plates soon separated and were collected (103 mg.); they included a few small reddish needles. Attempts to recrystallize the product from a large volume of ethanol converted it into vermilion-coloured needles which had no definite m. p. but charred slowly above 300° and were not molten at 350°. The sample partially sublimed in the m. p. tube at about 300°, giving dark red needles. The vermilion-coloured condensation product {7,10-*dihydroxy*-8,11 *dioxobenzo*[d]*cyclohepta*[3,4]*pyrrolo*[1,2-a]*imidazole* (IV) or the 6,9-*dihydroxy-isomer*} was difficult to purify and was virtually insoluble in the common organic solvents (Found: C, 63·6; H, 2·8; N, 9·6. $C_{15}H_8O_4N_2$ requires C, 64·2; H, 2·9; N, 10·0%). The brown crystalline intermediate condensation product (N-o-*aminophenyl*-3,6-*dihydroxy*-3-*oxocyclohepta*-1,5,6-*triene*-1,2-*dicarboxyimide*), decomp. >320°, was also difficult to purify and sparingly soluble in the common organic solvents (Found: N, 9·6. $C_{15}H_{10}O_5N_2$ requires N, 9·4%). It could not be recrystallized.

Fusion of Stipitatonic Acid with Potassium Hydroxide and Methylation of the Product.—Stipitatonic acid (80 mg.) was dissolved in water (1 ml.) in a nickel crucible, and potassium hydroxide (2 g.) added. The crucible was heated in a Woods-metal bath slowly and kept at a bath-temperature of 310° for 15 min., during which the melt remained clear, showing no tendency to char. After cooling, distilled water was added and the ice-cold solution acidified with hydrochloric acid. Continuous extraction in a liquid–liquid extractor with ether, drying of the extract (Na_2SO_4), and removal of the solvent afforded a white solid acid (70 mg.). Sublimation in a high vacuum gave first oxalic acid, m. p. and mixed m. p. 188°, then at 180° a pale yellow compact mass. This was probably an anhydride as it readily dissolved in water to a yellow, highly fluorescent solution which rapidly became colourless on gentle warming. The corresponding acid was obtained as white crystals, m. p. 278—281°, by removal of the water at room temperature. It gave an intense cherry-red colour with aqueous ferric chloride and a positive fluorescein reaction on fusion with resorcinol, but not by the wet reaction involving concentrated sulphuric acid. With ethereal diazomethane in the presence of methanol it afforded white crystals which sublimed in a high vacuum at 100°. Crystallization from ethanol gave trimethyl 6-methoxybenzene-1,2,4-tricarboxylate as prisms, m. p. 145°, identical in m. p., mixed m. p., and infrared absorption spectrum with a specimen prepared by Gardner *et al.*[13] (Berner[14] reports m. p. 144°) (Found: C, 55·6; H, 4·8. Calc. for $C_{13}H_{14}O_7$: C, 55·3; H, 5·0%).

The author is grateful to Dr. Yoshio Kitahara (Tohoku University, Sendai, Japan) for comparison of stipitatonic acid with synthetic specimens of 5-, 6-, and 7-hydroxytropolone-3,4-dicarboxylic anhydride, to Miss E. M. Tanner (Research Dept., Parke, Davis & Co. Ltd.)

[14] Berner, *J.*, 1946, 1052.

for determining the infrared absorption spectrum of stipitatonic acid, and to Mr. J. F. Grove (Imperial Chemical Industries Limited, Akers Research Laboratories) for an authentic specimen of trimethyl 6-methoxybenzene-1,2,4-tricarboxylate and for determining the infrared absorption spectrum of this compound derived from stipitatonic acid. This work has been done during the tenure of an Imperial Chemical Industries Research Fellowship.

BIOCHEMISTRY DEPARTMENT, LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, UNIVERSITY OF LONDON. [*Received, March 26th*, 1959.]

---

572. *Thiadiazoles. Part VIII.** 3-*Alkyl(or aryl)*-5-*alkyl(or aryl)*-*amino*-1,2,4-*thiadiazoles.*

By FREDERICK KURZER and W. TERTIUK.

N'-Substituted *N*-acetimidoyl- and *N*-benzimidoyl-thioureas are cyclised by oxidising agents to 3-alkyl(or aryl)-5-alkyl(or aryl)amino-1,2,4-thiadiazoles, some properties of which are described.

As part of an extension of the general synthesis [1,2] of 1,2,4-thiadiazoles by the cyclisation of compounds incorporating the amidinothiono-function, ·C(:NH)·NH·CS·, the oxidation of *N'*-substituted *N*-acimidoylthioureas has been examined. The reaction provides a useful route to the thiadiazole derivatives named in the title of this paper.

N'-Substituted *N*-benzimidoyl thioureas (I; R' = Ph) were readily synthesised from benzamidine and isothiocyanates in 70—80% yield by Pinner's method.[3] *N*-Acetimidoyl homologues (I; R' = Me) were obtained by the same procedure, though in greatly reduced yields (30—40%): the free bases were highly soluble in the aqueous ethanol used as reaction medium, but they were conveniently isolated as toluene-*p*-sulphonates. Attempts to improve yields by varying the conditions were not successful: in pyridine–triethylamine, acetamidine and phenyl isothiocyanate failed to react, *sym*-diphenylthiourea being the main product. The use of sodium alkoxides in acetone, a procedure that is particularly effective in the preparation of substituted amidinothioureas,[4-7] gave mainly *N*-acetyl-*N'*-phenylthiourea, by the hydrolytic conversion of the acetimidoyl- into the acetyl group, either before or after condensation of the base with the isothiocyanate. The well-known tendency of compounds of type (I) to undergo this change [8] is illustrated by the hydrolysis of *NN'*-bisphenylcarbamoylbenzamidine (Ph·NH·CO·N:CPh·NH·CO·NHPh, the condensation product of benzamidine and excess of phenyl isocyanate) to *N*-benzoyl-*N'*-phenylurea when attempts are made to crystallise it from acetic acid.[3]

N'-Substituted *N*-acimidoylthioureas (I), or their toluene-*p*-sulphonates, were rapidly cyclised by hydrogen peroxide or bromine under the usual conditions,[2,6,9] affording the corresponding 1,2,4-thiadiazoles (II) in excellent yields. The products were isolated directly, or, when their solubility made it desirable, as the toluene-*p*-sulphonates, from which the base was subsequently liberated. The highly soluble low-melting 5-*n*-butylamino-3-methyl homologue (II; R = Bu^n, R' = Me) was obtained as the picrate and picrolonate only.

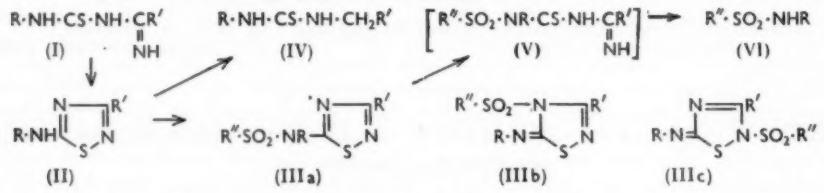
Two representatives of the series of thiadiazoles (II) now described have previously

* Part VII, Kurzer and Taylor, *J.*, 1959, 1064.

[1] Ishikawa, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, 1928, **7**, 237.
[2] Kurzer, *J.*, 1955, 1, and subsequent papers.
[3] Pinner, *Ber.*, 1889, **22**, 1600, 1609.
[4] Slotta, Tschesche, and Drechsler, *Ber.*, 1930, **63**, 208.
[5] Kurzer, *J.*, 1955, 2288.
[6] Kurzer, *J.*, 1956, 2345.
[7] Kurzer, *J.*, 1957, 2999.
[8] Cf. also Pinner and Klein, *Ber.*, 1878, **11**, 6; Pinner, "Die Imidoäther und Ihre Derivate," Oppenheim, Berlin, 1892, p. 155.
[9] Kurzer and Taylor, *J.*, 1958, 379; *J.*, 1959, 1064.

XUM

been prepared by other methods and are identical with specimens obtained by the present synthesis. 5-Anilino-3-phenyl-1,2,4-thiadiazole has been obtained by the condensation of benzamidoformaldoxime and phenyl isothiocyanate in chloroform [10] or ethanol,[11] by the interaction of *N*-benzenesulphenylbenzamidine and phenyl isothiocyanate,[12] and,



from the pre-formed heterocyclic system, by the action of aniline on 5-mercapto-3-phenyl-1,2,4-thiadiazole.[13,14] 5-Methylamino-3-phenyl-1,2,4-thiadiazole results from the action of methylamine on the 5-chloro-analogue,[15] which is in turn accessible from benzamidine and trichloromethanesulphenyl chloride ($Cl_3C{\cdot}SCl$).[16] The synthesis of 3-substituted-5-alkyl(or aryl)amino-1,2,4-thiadiazoles (II) now reported provides compounds of unequivocal structure and appears to possess advantages over previous methods because of its wide applicability, the ready availability of the starting materials, and the consistently good yields.

Like most substituted 3,5-diamino-[5,6] and 5-amino-3-hydroxy(or mercapto)-1,2,4-thiadiazoles,[9] 5-phenyl homologues were unaffected by boiling aqueous alkali in the presence of sodium plumbite, but members of the 3-methyl series were gradually desulphurised by this reagent. Acimidoylthioureas (I) were, of course, decomposed almost instantly under these conditions, with deposition of lead sulphide.

5-Anilino-3-phenyl-1,2,4-thiadiazole gave a monoacetyl [10] and a monobenzoyl derivative but failed to react with toluene-*p*-sulphonyl chloride. A monotoluene-*p*-sulphonyl derivative was, however, obtained from 5-anilino-3-methyl-1,2,4-thiadiazole, and gave substantially toluene-*p*-sulphonanilide on reductive hydrolysis, thus establishing structure (IIIa; R = Ph, R′ = Me, R″ = *p*-Me·C_6H_4) for the sulphonyl derivative. The observation that a sulphonyl halide reacts preferentially at the 5-anilino-group in a thiadiazole of type (II) provides the basis for assigning structures (IIIa; R = Me or Ph, R′ = *p*-Me·C_6H_4·SO_2·NH, R″ = *p*-Me·C_6H_4) to the ditosyl derivatives (m. p. 171—173° and 204—205° respectively) of 3-amino-5-methylamino [5] (or anilino [6])-1,2,4-thiadiazole which had previously remained undecided. Further, in the light of this evidence, the disulphonyl derivative [6,7] (m. p. 240—242°) of 3,5-dianilino-1,2,4-thiadiazole may have the 3,5-di-(*N*-toluene-*p*-sulphonanilido)- rather than the structure first [6] suggested, and the site of the substituents in the corresponding trisulphonyl derivatives [5,6] may require reconsideration.

The failure of certain 1,2,4-thiadiazoles (*e.g.*, II; R = Ph, R′ = MeO,[9] MeS,[9] or Ph) to react with sulphonyl chlorides under the usual conditions is not due to steric effects, because of the existence of sulphonyl derivatives of 5-anilino-3-methyl- and 3,5-dianilino-1,2,4-thiadiazole. Since they all yield acetyl and benzoyl derivatives, a consistently parallel behaviour of 1,2,4-thiadiazoles towards acylating agents and sulphonyl halides cannot be assumed, and it is therefore inadmissible to assign structures to acyl derivatives from a knowledge of those of sulphonyl compounds alone. A choice between possible formulations of monoacyl derivatives (analogues of IIIa–c) of thiadiazoles (II) is therefore deferred, as is that of several similar derivatives previously described.[5,6,9]

[10] Koch, *Ber.*, 1891, **24**, 394.
[11] Gheorghiu and Barbos, *Ann. Sci. Univ. Jassy*, 1940, **26**, I, 271.
[12] Goerdeler, Krause-Loevenich, and Wedekind, *Chem. Ber.*, 1957, **90**, 1638.
[13] Crayen, *Ber.*, 1891, **24**, 385.
[14] Barbos, *Ann. Sci. Univ. Jassy*, 1940, **26**, I, 526.
[15] Goerdeler, Huppertz, and Wember, *Chem. Ber.*, 1954, **87**, 68.
[16] Goerdeler, Groschopp, and Sommerlad, *Chem. Ber.*, 1957, **90**, 182.

On treatment with zinc and hydrochloric acid, 5-anilino-3-phenyl-1,2,4-thiadiazole (II; R = R′ = Ph) was slowly converted into *N*-benzyl-*N*′-phenylthiourea (IV; R = R′ = Ph), probably by the usual ring opening at the N–S bond,[2,5,6,7,9] followed by further reductive hydrolysis of the intermediate (I; R = R′ = Ph) to (IV). This interpretation agrees with the observation that *N*-benzimidoyl-*N*′-phenylthiourea also afforded *N*-benzyl-*N*′-phenylthiourea under identical conditions. However, the reduction was much slower and less complete than the smooth and rapid comparable conversion of substituted 3,5-diamino-1,2,4-thiadiazoles into amidinothioureas,[2,6] or of 5-anilino-3-hydroxy-1,2,4-thiadiazole into 1-phenyl-2-thiobiuret,[9] suggesting an enhanced stability of (II; R = R′ = Ph). It also differed from the comparable reduction of 3,5-diphenyl-1,2,4-thiadiazole to *N*-benzylbenzamidine [17,18] in that the amidinothiono-group of the intermediate was reduced at the imino- and not the thiocarbonyl centre, a fact that may be due to its different structural environment in the two compounds. The analogous reduction of the imino-function of a substituted amidine has been observed in the slow and incomplete conversion of *NN*-diethylbenzamidine into benzylamine [19] by lithium aluminium hydride.

Experimental

The pyridine used was the commercially available anhydrous grade. Light petroleum was of boiling range 60—80°. Cellosolve was 2-ethoxyethanol (technical). The solvent used for preparing M-bromine was chloroform. Amalgamated zinc was prepared by heating zinc shavings with 3N-sodium hydroxide until hydrogen was freely evolved, washing the metal with distilled water, treating it with 1% aqueous mercuric chloride at 40°, and rinsing it successively with distilled water and ethanol.

N-Benzimidoyl-N′-phenylthiourea.—This was prepared by the method outlined by Pinner [9] as follows: To a solution of benzamidine hydrochloride [20] (15·65 g., 0·1 mole) in warm water (20 ml.), cooled to room temperature, phenyl isothiocyanate (13·5 g., 0·1 mole) was added, followed by ethanol (120 ml.), until a one-phase system was obtained. Addition of 3N-sodium hydroxide (33·3 ml., 0·1 mole) gave a clear yellow liquid, the temperature of which rose slightly temporarily. Lustrous yellow prisms separated rapidly, were collected after 12 hours' storage at 0°, and washed with a little cold ethanol [m. p. 122—124° (decomp.); 19·1—20·9 g., 75—82%]. Evaporation of the filtrates in a vacuum to small bulk afforded further small quantities (up to 5%) of the product, but unidentified high-melting (~240—250°) by-products were isolated in some experiments. Two crystallisations from ethanol (8 ml. per g.) gave lustrous pale-yellow prisms of the thiourea, m. p. 124—125° (decomp.) (Found: C, 65·4; H, 4·9. Calc. for $C_{14}H_{13}N_3S$: C, 65·9; H, 5·1%).

N-Benzimidoyl-N′-p-tolylthiourea.—This was obtained by the same procedure from benzamidine hydrochloride (0·05 mole), water (10 ml.), *p*-tolyl isothiocyanate (7·45 g., 0·05 mole), ethanol (90 ml.), and 3N-sodium hydroxide (0·05 mole) as massive yellow prisms (10·75 g., 80%). Two crystallisations from ethanol (8 ml. per g.) gave pale-yellow prisms of the *thiourea*, m. p. 112—113° (decomp.) (Found: C, 66·1; H, 5·8. $C_{15}H_{15}N_3S$ requires C, 66·9; H, 5·6%).

N-Benzimidoyl-N′-methylthiourea was similarly obtained from benzamidine hydrochloride (0·05 mole), water (10 ml.), methyl isothiocyanate (3·65 g., 0·05 mole), ethanol (35 ml.), and 3N-sodium hydroxide (0·05 mole), and formed colourless prisms (6·75 g., 70%). Crystallisation from ethanol–light petroleum (6 and 4 ml. respectively per g.) gave lustrous prisms, m. p. 97—99° (decomp.) (Found: C, 56·0; H, 5·5; N, 22·2. $C_9H_{11}N_3S$ requires C, 56·0; H, 5·7; N, 21·8%).

N-Acetimidoyl-N′-phenylthiourea.—Acetamidine hydrochloride [20] (14·1 g., 0·15 mole) was dissolved in ethanol (100 ml.) with warming; the solution was treated, at room temperature, successively with phenyl isothiocyanate (20·25 g., 0·15 mole), 3N-sodium hydroxide (50 ml., (0·15 mole), and more ethanol (20 ml.) to produce a homogeneous liquid, which was set aside at room temperature during 12 hr. A small quantity of a white infusible product (1—2 g.)

[17] Hofmann and Gabriel, *Ber.*, 1892, **25**, 1578.
[18] Ishikawa, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, 1925, **3**, 147.
[19] Gilsdorf and Nord, *J. Amer. Chem. Soc.*, 1952, **74**, 1855.
[20] Dox, *Org. Synth.*, Coll. Vol. I, 1941, p. 5, 6.

XUM

which separated was removed, and the yellowish-green filtrate treated with toluene-*p*-sulphonic acid (monohydrate; 34·2 g., 0·18 mole; dissolved in 30 ml. of water). After a transient colour-change to deep-brown, the pale-yellow liquid deposited prisms (25 g.), which were collected at 0° and rinsed with a little ethanol (filtrate A). Crystallisation from 90% ethanol (6—8 ml. per g.) gave prisms (16·4—19·2 g., 30—35%) of *N-acetimidoyl-N′-phenylthiourea toluene-p-sulphonate*, m. p. 170—172° (decomp., somewhat subject to the rate of heating). Evaporation of the filtrates in a vacuum at <40° increased the yield of the salt by 3—6% (Found: C, 52·9; H, 5·0; N, 11·5; S, 17·7. $C_9H_{11}N_3S,C_7H_8O_3S$ requires C, 52·6; H, 5·2; N, 11·5; S, 17·5%). Filtrate A did not afford more crude material on either vacuum-evaporation or dilution with water.

The toluene-*p*-sulphonate (1·83 g., 0·005 mole), suspended in hot water (10 ml.) and treated with 3N-sodium hydroxide (2 ml., 0·006 mole) or 3N-ammonia (5 ml., 0·015 mole), gave a clear solution which deposited an oil on rapid cooling. The solidified oil gave, on crystallisation from ethanol (8 ml. per g.), platelets of *N-acetimidoyl-N′-phenylthiourea*, m. p. 153—154° (0·43—0·53 g., 45—55%) [Found: C, 55·4; H, 5·6; N, 21·3%; *M* (cryoscopically in thymol), 180. $C_9H_{11}N_3S$ requires C, 56·0; H, 5·7; N, 21·8%; *M*, 193].

Interaction of acetamidine hydrochloride (0·01 mole) and phenyl isothiocyanate (0·01 mole) in pyridine (20 ml.)–triethylamine (5 ml.) at 100° during 3 hr., followed by addition of the reaction mixture to ice–hydrochloric acid, gave mainly *sym*-diphenylthiourea, m. p. and mixed m. p. 153° (43%).

N-Acetyl-N′-phenylthiourea.—To the suspension obtained on introducing sodium (0·345 g., 0·015 g.-atom) into anhydrous acetone (50 ml.), a solution of acetamidine hydrochloride (1·42 g., 0·015 mole) in hot Cellosolve (6 ml.) was added, followed by phenyl isothiocyanate (2·03 g., 0·015 mole). The suspension was refluxed during 5 min., distilled in a vacuum to small volume during 5 min., stirred into water (150 ml.), and acidified (to Congo Red) with concentrated hydrochloric acid. The crystalline precipitate (m. p. 165—167°; 1·96 g., 67%) gave, on purification from ethanol, plates of *N*-acetyl-*N′*-phenylthiourea, m. p. and mixed m. p. with authentic material [21] 170—171° (Found: C, 55·8; H, 5·1; N, 13·9; S, 16·1. Calc. for $C_9H_{10}ON_2S$: C, 55·7; H, 5·15; N, 14·4; S, 16·5%).

N-Acetimidoyl-N′-p-tolylthiourea.—The procedure described for the phenyl homologue gave a crude product (m. p. 158—160°; 40%) which consisted, after crystallisation from ethanol (10 ml. per g., 75% recovery), of platelets of *N-acetimidoyl-N′-p-tolylthiourea toluene-p-sulphonate*, m. p. 165—167° (Found: C, 53·4; H, 5·65. $C_{10}H_{13}N_3S,C_7H_8O_3S$ requires C, 53·8; H, 5·5%).

N-Acetimidoyl-*N′*-butylthiourea was prepared (from 0·05 mole of each of the appropriate reagents, all in 50 ml. of ethanol) by the same procedure. After storage during 24 hr., the white powdery by-product was filtered off, and the colourless filtrate treated with toluene-*p*-sulphonic acid monohydrate (0·06 mole). Slow separation of silky needles was completed by storage at −8°, and the collected product (6·55 g., 38%) (filtrate F) crystallised from ethanol (8 ml. per g.) to yield needles (26%) of *N-acetimidoyl-N′-butylthiourea toluene-p-sulphonate*, m. p. 173—174° (Found: C, 49·2; H, 7·1; N, 12·0; S, 18·1. $C_7H_{15}N_3S,C_7H_8O_3S$ requires C, 48·7; H, 6·7; N, 12·2; S, 18·55%). Spontaneous evaporation of filtrates F gave large prismatic needles (1·80 g.) of non-homogeneous material from which no more of the desired thiourea could be isolated.

5-Anilino-3-phenyl-1,2,4-thiadiazole.—(a) *Oxidation by hydrogen peroxide.* A boiling solution of *N*-benzimidoyl-*N′*-phenylthiourea (12·75 g., 0·05 mole) in ethanol (180 ml.) was treated with a mixture of 6% hydrogen peroxide (71 ml., 0·125 mole) and concentrated hydrochloric acid (5 ml., 0·05 mole) during 8—10 min. Towards the end of the addition the yellow colour of the solution was discharged, and crystals appeared, the separation of which was completed by storage at 0° during 4 hr. The collected washed (ethanol) product (m. p. 170—172°; 9·5—10·4 g., 75—82%) was crystallised from ethanol (15 ml. per g.), and consisted of platelets of 5-anilino-3-phenyl-1,2,4-thiadiazole, m. p. 173—174° [Found: C, 66·2; H, 4·2; N, 16·4; S, 12·4%; *M* (cryoscopically, in thymol), 245. Calc. for $C_{14}H_{11}N_3S$: C, 66·4; H, 4·35; N, 16·6; S, 12·65%; *M*, 253]. (b) *Oxidation by bromine.* A solution of *N*-benzimidoyl-*N′*-phenylthiourea (2·55 g., 0·01 mole) in cold chloroform (12 ml.) decolorised M-bromine (10 ml., 0·01 mole) as fast as it was added. The liquid was evaporated in a vacuum at low temperatures to small bulk, and the residual suspension shaken with water (50 ml.). The chloroform and the aqueous layer were separated, and later recombined when all the chloroform had evaporated spontaneously. The

[21] Dixon and Hawthorne, *J.*, 1907, **91**, 128, 130.

collected white solid, on crystallisation from ethanol as above, gave platelets of the 1,2,4-thiadiazole (total, 2·28 g., 90%), m. p. and mixed m. p. with material obtained by method (a) 173—174°. The m. p. of 5-anilino-3-phenyl-1,2,4-thiadiazole given in the literature [10,11,14,12] is 174—176°.

Reduction. To a boiling solution of the reactant (3·80 g., 0·015 mole) in ethanol (75 ml.) containing zinc shavings (8 g.), concentrated hydrochloric acid (8 ml.) was added dropwise during 1 hr., and refluxing continued during a total of 2·5 hr. (another 2 ml. of acid being added after 2 hours' boiling). The decanted liquid (together with 20 ml. of boiling ethanol, used to re-extract the residual zinc) was evaporated in a vacuum (to 15 ml.), set aside at 0° during 2 hr. (Note N), then stirred into water, and the white soft product (2·5 g.) was dissolved in benzene (20 ml.)–acetone (5 ml.). The filtered liquid was set aside for spontaneous evaporation, the solvent being gradually replaced by ethanol. The separated product (m. p. ~140°; 1·5—2·0 g.) crystallised from ethanol (12 ml. per g.) as prisms (1·27—1·65 g., 35—45%) of *N*-benzyl-*N'*-phenylthiourea, m. p. and mixed m. p. 151—152° (Found: C, 69·8; H, 6·0; N, 11·0; S, 12·8. Calc. for $C_{14}H_{14}N_2S$: C, 69·4; H, 5·8; N, 11·6; S, 13·2%). Use of amalgamated zinc did not improve yields.

Note N: In experiments involving a shorter time of refluxing starting material separated from this solution and was removed by filtration at this stage: yields of the thiourea were lowered correspondingly.

Reduction of N-*Benzimidoyl*-N'-*phenylthiourea.*—This compound (3·80 g., 0·015 mole) was reduced as described immediately above. The crude resinous product was dissolved in benzene (20 ml.), the liquid allowed to evaporate to dryness, and the filtered solution of the remaining gum in ethanol (10 ml.) stirred into ice. The soft dry product was redissolved in ethanol (10 ml.); the sticky viscous liquid slowly deposited a white powder (0·85—1 g.) which gave *N*-benzyl-*N'*-phenylthiourea, m. p. and mixed m. p. 151—152° (from ethanol) (0·63 g., 17%).

N-*Benzyl*-N'-*phenylthiourea.*—Benzylamine (3·2 g., 0·03 mole) in pyridine (15 ml.) was treated with phenyl isothiocyanate (3·4 g., 0·025 mole), and the liquid was kept at 100° during 30 min., then poured into ice and hydrochloric acid. The precipitate, crystallised from ethanol (10 ml. per g.), consisted of prisms of the thiourea, m. p. 152—153° (5·55 g., 92%). The m. p. of *N*-benzyl-*N'*-phenylthiourea is given in the literature [19,22] variously between 153° and 158°.

Derivatives.—5-Anilino-3-phenyl-1,2,4-thiadiazole (1·27 g., 0·005 mole), dissolved in pyridine (10 ml.), was treated with acetic anhydride (3·05 g., 0·03 mole), and the solution kept at 100° for 0·5 hr. and stirred into ice (100 g.) and concentrated hydrochloric acid (12 ml.). The washed dried precipitate was crystallised from acetone–ethanol, and gave prisms of the monoacetyl derivative, m. p. 202—204° (0·98 g., 67%) (Found: C, 64·8; H, 4·5; N, 14·35; S, 10·9. Calc. for $C_{16}H_{13}ON_3S$: C, 65·1; H, 4·4; N, 14·2; S, 10·85%). Koch [10] gives m. p. 196°. Interaction of the thiadiazole (0·005 mole) with benzoyl chloride (2·10 g., 0·015 mole) under the same conditions, and crystallisation of the crude product from acetone–ethanol, gave needles of the *monobenzoyl derivative*, m. p. 177—178° (decomp.) (1·45 g., 81%) (Found: C, 70·6; H, 4·05; N, 11·2. $C_{21}H_{15}ON_3S$ requires C, 70·6; H, 4·2; N, 11·8%). 5-Anilino-3-phenyl-1,2,4-thiadiazole (0·005 mole) was recovered unchanged (85 and 65% respectively) after being heated at 100° with toluene-*p*-sulphonyl chloride (0·015 mole during 0·5 hr., or 0·03 mole during 3 hr.) in pyridine (15 ml.).

3-*Phenyl*-5-p-*tolylamino*-1,2,4-*thiadiazole.*—Oxidation of *N*-benzimidoyl-*N'*-*p*-tolylthiourea (2·69 g., 0·01 mole) in boiling ethanol (45 ml.) by method (a), and crystallisation of the separated white product (m. p. 152—154°; 2·06 g., 77%) from ethanol (20 ml. per g.), afforded the 1,2,4-*thiadiazole* as platelets (65%), m. p. 156—157° (Found: C, 67·2; H, 4·7; N, 15·3. $C_{15}H_{13}N_3S$ requires C, 67·4; H, 4·9; N, 15·7%).

5-*Methylamino*-3-*phenyl*-1,2,4-*thiadiazole.*—*N*-Benzimidoyl-*N'*-methylthiourea (1·93 g., 0·01 mole) in boiling ethanol (15 ml.), on oxidation by method (a), gave crystals (m. p. 154—156°; 1·6 g., 84%) which afforded, after crystallisation from ethanol (15 ml. per g.), prisms of the 1,2,4-thiadiazole, m. p. 155—157° (Found: C, 56·2; H, 4·6; N, 21·6. Calc. for $C_9H_9N_3S$: C, 56·5; H, 4·7; N, 22·0%). Goerdeler *et al.*[15] give m. p. 157°.

5-*Anilino*-3-*methyl*-1,2,4-*thiadiazole.*—(a) *Oxidation by hydrogen peroxide.* A boiling solution of *N*-acetimidoyl-*N'*-phenylthiourea toluene-*p*-sulphonate (7·3 g., 0·02 mole) in 90% ethanol

[22] Dixon, *J.*, 1889, **55**, 301; Beckmann, *J. prakt. Chem.*, 1897, **56**, 88; Campbell, Campbell, and Patelski, *Proc. Indiana Acad. Sci.*, 1943, **53**, 119; Weller, Ball, and Sell, *J. Amer. Chem. Soc.*, 1952, **74**, 1104; Horner and Gross, *Annalen*, 1955, **591**, 117.

XUM

(50 ml.) was treated, during 3—4 min., with a mixture of 6% hydrogen peroxide (28·5 ml., 0·05 mole) and concentrated hydrochloric acid (2 ml., 0·02 mole), and continued to be boiled during another 2 min. The faintly purple turbid liquid was added to ice-water (200 ml.) and basified with 3N-ammonia (40 ml.). The precipitated solid (which tended to become dark grey on prolonged storage) was collected after 12 hours' storage at 0° [m. p. 109—111° (decomp.); 2·1—2·5 g., 55—65%] (Filtrate: M). The material was crystallised by diluting its filtered ethanolic solution (5 ml. per g.), previously treated at its b. p. with carbon during 5 min., with an equal volume of hot water and formed prismatic needles of *5-anilino-3-methyl-1,2,4-thiadiazole*, m. p. 113—114°, appreciably soluble in boiling water [Found: C, 56·3; H, 4·65; N, 22·2%; *M* (cryoscopically, in thymol), 197. $C_9H_9N_3S$ requires C, 56·5; H, 4·7; N, 22·0%; *M*, 191]. Partial evaporation of filtrate M did not afford more of the required thiadiazole. The dark residue, on crystallisation from ethanol (carbon) gave small quantities of unidentified material (m. p. 195—196°; 0·3—0·4 g.). The use of a larger excess of hydrogen peroxide (3 mols), slightly increased times of reaction (10—12 min.), or prolonged storage of the final reaction mixture, gave lower yields of dark brown to grey crude products, which were purified with greater difficulty by the use of muchcarbon.

(b) *Oxidation by bromine.* The reactant (3·65 g., 0·01 mole) was dissolved in 90% ethanol (50 ml.) with warming, the cooled (approx. 30—35°) solution treated with M-bromine (10 ml., 0·01 mole) (small quantities of crystals which may have separated, redissolved during this addition) and rapidly concentrated to small volume (12—15 ml.) by vacuum-distillation. To the residual colourless liquid, diluted with water (8 ml.), toluene-*p*-sulphonic acid monohydrate (3·80 g., 0·02 mole) was added and dissolved rapidly. The crystals which separated on storage at −8° were collected (1·55—1·7 g.) (filtrate: N) and crystallised from absolute ethanol, forming needles (1·16 g., 32%) of *5-anilino-3-methyl-1,2,4-thiadiazole toluene-p-sulphonate*, m. p. 154—156° (decomp.) (Found: C, 53·2; H, 4·9; N, 11·2. $C_{16}H_{17}O_3N_3S_2$ requires C, 52·9; H, 4·7; N, 11·6%). Spontaneous evaporation of filtrates N to small volume gave syrups that deposited only small quantities (0·2—0·4 g.) of non-homogeneous crystals.

A suspension of the toluene-*p*-sulphonate (0·91 g., 0·0025 mole) in 3N-ammonia (10 ml.) was heated to boiling with good shaking. The resulting suspended oil set to a white granular solid on cooling, and more crystalline product was deposited at 0°. The collected crude base (m. p. 111—114°; 0·41 g., 86%) crystallised as before and formed needles of 5-anilino-3-methyl-1,2,4-thiadiazole, m. p. and mixed m. p. 113—114°.

3-Methyl-5-toluene-p-sulphonanilido-1,2,4-thiadiazole.—A solution of 5-anilino-3-methyl-1,2,4-thiadiazole (1·91 g., 0·01 mole) in pyridine (25 ml.), treated with toluene-*p*-sulphonyl chloride (7·6 g., 0·04 mole), was kept on the steam-bath during 1½ hr. The dark viscous liquid was stirred into ice (100 g.) and concentrated hydrochloric acid (25 ml.), and the solidified dark-brown precipitate was extracted with 1·5N-sodium hydroxide at 50° during 15 min. (removal of excess of sulphonyl chloride), collected, washed with water, and crystallised from boiling ethanol (10 ml. per g., with addition of carbon–kieselguhr). The light brown filtrate deposited nearly colourless needles of the *toluene-p-sulphonyl derivative*, m. p. 160—161° (after a further crystallisation) (total, including material from mother-liquors, 2·25 g., 65%) (Found: C, 55·7; H, 4·5; N, 12·4; S, 18·8. $C_{16}H_{15}O_2N_3S_2$ requires C, 55·65; H, 4·35; N, 12·2; S, 18·55%).

Reduction.—A solution of the preceding compound (0·69 g., 0·002 mole) in ethanol (25 ml.) containing amalgamated zinc (2 g.) was refluxed during 2 hr. and treated dropwise with concentrated hydrochloric acid (2 × 3 ml.) during the first and third half-hour. The decanted liquid, together with washing alcohol (8 ml.) used in extracting the zinc a second time, was distilled in a vacuum to small volume (5 ml.), and the residue stirred into water. The solidified precipitate (m. p. 98—99°; 0·305 g., 62%) smelled strongly of thiocresol, but was almost pure toluene-*p*-sulphonanilide, m. p. and mixed m. p. 99—100° (prisms, from benzene–light petroleum). The reactant was recovered (75%) after 15 minutes' treatment with zinc (non-amalgamated) and hydrochloric acid under the above conditions.

3-Methyl-5-p-tolylamino-1,2,4-thiadiazole.—This *base* was prepared from *N*-acetimidoyl-*N'*-*p*-tolylthiourea toluene-*p*-sulphonate (3·8 g., 0·01 mole) (as described for the 5-anilino-homologue, method *a*). The crude product (m. p. 134—136°; 1·75 g., 85%) afforded, on crystallisation from ethanol (10 ml. per g.), elongated prisms, m. p. 136—137° (Found: C, 58·4; H, 5·1. $C_{10}H_{11}N_3S$ requires C, 58·5; H, 5·4%).

5-n-Butylamino-3-methyl-1,2,4-thiadiazole.—*N*-Acetimidoyl-*N'*-butylthiourea toluene-*p*-sulphonate (0·01 mole) in ethanol (12 ml.) was oxidised (as described for the 5-anilino-analogue,

method *a*), the resulting turbid liquid filtered under reduced pressure (double filter-paper), and the filtrate divided into two equal portions. One half, treated with a solution of picric acid (1·145 g., 0·005 mole) in ethanol (10 ml.) and set aside at 0°, gave the *picrate* (1·78 g., 45%; cf. Table). The other half, treated with picrolonic acid (1·32 g., 0·005 mole) in ethanol (25 ml.), gradually diluted with water (20 ml.), and set aside at 0°, deposited yellow crystals, m. p. 134—136° (decomp.) (1·25 g., 29%) (filtrate F), which on crystallisation from ethanol gave yellow needles of the *picrolonate*, m. p. 133—135° (Found: C, 47·35; H, 4·9. $C_7H_{13}N_3S,C_{10}H_8O_5N_4$ requires C, 46·9; H, 4·8%). Spontaneous evaporation of filtrate F gave more yellow solid (m. p. 110°), which afforded additional picrolonate (8%) on crystallisation (combined yield of thiadiazole, 82%). The base was low-melting and water-soluble: it was extractable by ether, but was not isolated pure.

Picrates of N′*-substituted* N*-acimidoylthioureas*, R·NH·CS·NH·CR′(:NH),$C_6H_3O_7N_3$.

				Found (%)		Required (%)	
R′	R	M. p.*	Formula	C	H	C	H
Ph	Me	175—176°	$C_{15}H_{14}O_7N_6S$	42·7	3·4	42·65	3·3
Ph	Ph	209—210	$C_{20}H_{16}O_7N_6S$	49·95	4·3	49·6	3·3
Ph	*p*-Tolyl	210—211	$C_{21}H_{18}O_7N_6S$	50·9	3·5	50·6	3·6
Me	Ph	211—212	$C_{15}H_{14}O_7N_6S$	42·9	3·1	42·65	3·3
Me	*p*-Tolyl	150—152	$C_{16}H_{16}O_7N_6S$	44·4	3·75	44·0	3·7

Picrates of 3*-alkyl(aryl)-*5*-alkyl(aryl)amino-*1,2,4*-thiadiazoles*, 3-R′-5-R·NH·C_2N_2S,$C_6H_3O_7N_3$

Ph	Me	143—144	$C_{15}H_{12}O_7N_6S$	42·9	2·6	42·9	2·9
Me	Bu^n	138—139	$C_{13}H_{16}O_7N_6S$	39·4	3·7	39·0	4·0
Me	Ph	163—164	$C_{15}H_{12}O_7N_6S$	43·1	3·0	42·9	2·9
Me	*p*-Tolyl	184—185	$C_{16}H_{14}O_7N_6S$	44·5	3·0	44·2	3·2

* Decomp. on melting.

Picrates of *N*′-substituted *N*-benzimidoylthioureas and 3-alkyl(or aryl)-5-alkyl(or aryl)-amino-1,2,4-thiadiazoles were obtained, in 70—90% yield, as deep yellow to orange prisms, from equimolar proportions of the components (0·002 mole) in hot ethanol (12—20 ml.). *N*′-Substituted *N*-acetimidoylthiourea picrates resulted in somewhat lower yields (55—65%) from solutions of the toluene-*p*-sulphonates in 90% ethanol and ethanolic picric acid.

N-Acetimidoyl-*N*′-*n*-butylthiourea, 5-anilino-3-phenyl-1,2,4-thiadiazole, and 3-phenyl-5-*p*-tolylamino-1,2,4-thiadiazole failed to yield picrates, the starting material being recovered.

Sodium Plumbite Tests.—Solutions or suspensions of the compound (approx. 0·1 g.) under examination in 3N-sodium hydroxide (3 ml.) were treated with 3 drops of 10% lead acetate and boiled. All substituted thioureas (I) gave immediate copious precipitates of lead sulphide as soon as the liquid began to boil. 3-Methyl-1,2,4-thiadiazoles (II; R = Bu^n, Ph, or *p*-Me·C_6H_4, R′ = Me) slowly deposited sulphide after 2—3 min.; 3-phenyl homologues (II; R = Me, Ph, or *p*-Me·C_6H_4, R′ = Ph) failed to do so on prolonged boiling.

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE,
(UNIVERSITY OF LONDON), W.C.1.

[*Received, April 13th*, 1959.]

XUM

573. *Synthesis of Some Phenyl-cinnolines, -phthalazines, and -quinoxalines.*

By C. M. Atkinson and C. J. Sharpe.

Unambiguous routes to 3-, 6-, and 7-phenylcinnoline, to 5- and 6-phenylquinoxaline, and to 6-phenylphthalazine are described. 4-Hydroxycinnolines have been reduced with lithium aluminium hydride.

An improved method for carrying out the Gomberg reaction is reported.

Authentic phenyl derivatives of bicyclic diazines were required in connection with work on the phenylation of the corresponding heterocyclic compounds. For the preparation of 5- and 6-phenylquinoxaline, 2 : 3- and 3 : 4-diaminodiphenyl, respectively, were required. The first of these intermediates has been reported [1] only as the unstable, oily hydrochloride. Nitration of 2-acetamidodiphenyl by the improved method of Stepan and Hamilton [2] and chromatography of the mixed nitro-amines has given a much purer sample of 2-amino-3-nitrodiphenyl; this yielded by catalytic reduction the crystalline diamine. Attempts to hydrolyse 2-acetamido-3-aminodiphenyl with acid or alkali gave a common product, presumably 2-methyl-7-phenylbenzimidazole.[3] The route to 4-amino-3-nitrodiphenyl from 4-nitrodiphenyl has been well described,[4] and catalytic reduction of both of these compounds assured an excellent overall yield.

4-Phenylphthalazine is known,[5] and for the synthesis of 5- and 6-phenylphthalazine there were required 3- and 4-phenylphthalic acid: these have been obtained [6] in about 35% yield by means of a Gomberg reaction on the dimethyl esters of the corresponding amines. In the present work, this yield has been improved to about 60% by carrying out the diazotisation with butyl nitrite, causing the product to react in benzene by addition of anhydrous sodium carbonate, and hydrolysing the insoluble intermediates. An alternative route to 3-phenylphthalic anhydride by a Diels–Alder reaction between 1-phenylbutadiene and maleic anhydride [7] was unsuccessful. The adduct could not be wholly dehydrogenated with sulphur, selenium, or *N*-bromosuccinimide; it was recovered from treatment with chloranil at low temperatures, and at high temperatures only halogeno-compounds appeared to be formed. The catalytic hydrogen-transfer method using palladised charcoal in alcohol with nitrobenzene or nitromethane also failed to bring about dehydrogenation.

Reaction of 3-phenylphthalic acid or the anhydride with hydrazine did not yield the expected 1 : 4-dihydroxy-5-phenylphthalazine; instead, a compound was obtained arising from the condensation of two molecules of acid with one of hydrazine: this formulation is supported by the analytical figures and by the behaviour of phthalic anhydride itself with hydrazine.[8] An attempt to prepare the bis-acid chloride from 3-phenylphthalic anhydride and phosphorus pentachloride [9] yielded only fluorenone-3-carboxylic acid.[6] 4-Phenylphthalic acid reacted smoothly with hydrazine to form 1 : 4-dihydroxy-6-phenylphthalazine, which was converted into the 1 : 4-dichloro-derivative: reduction of this with red phosphorus and hydriodic acid gave a low yield of 6-phenylphthalazine.

Of the six possible monophenylcinnolines, only 4-phenylcinnoline has been previously prepared.[10] For the preparation of 7-phenylcinnoline, 4-amino-3-nitrodiphenyl was converted into 4-cyano-3-nitrodiphenyl through the diazonium compound, which we found

[1] Sako, *Bull. Chem. Soc. Japan*, 1934, **9**, 55.
[2] Stepan and Hamilton, *J. Amer. Chem. Soc.*, 1949, **71**, 2438.
[3] Hofmann, "Imidazole and its derivatives," Interscience Publ. Inc., New York, 1953, p. 264.
[4] Campbell, Anderson, and Gilmore, *J.*, 1940, 446.
[5] Lieck, *Ber.*, 1905, **38**, 3918.
[6] Butterworth, Heilbron, Hey, and Wilkinson, *J.*, 1938, 1386.
[7] Kharasch, Nudenberg, and Fields, *J. Amer. Chem. Soc.*, 1944, **66**, 1276.
[8] Drew and Hatt, *J.*, 1937, 16.
[9] Ott, *Org. Synth., Coll. Vol. II*, p. 528.
[10] Stoermer and Fincke, *Ber.*, 1909, **42**, 3115.

more convenient to prepare by using nitrosylsulphuric acid rather than butyl nitrite.[11] The corresponding amino-nitrile and amino-amide were prepared by recorded methods,[11] but neither compound reacted with methylmagnesium iodide. Attempts to hydrolyse 4-cyano-3-nitrodiphenyl directly to the acid failed, but by proceeding *via* the nitroamide a high overall yield of 2-nitro-4-phenylbenzoic acid was obtained. The general method of Walker and Hauser [12] was used to convert this acid into the methyl ketone, from which 4-hydroxy-7-phenylcinnoline was obtained by reduction, diazotisation, and cyclisation.

2-Nitro-5-phenylacetophenone, required for the preparation of 4-hydroxy-6-phenylcinnoline, was synthesised from 5-amino-2-nitroacetophenone [13] by the usual Gomberg procedure in a yield of only 4%, and attempts to prepare (for subsequent decomposition) 2-nitro-5-*N*-nitrosoacetamidoacetophenone with nitrous fumes or nitrosyl chloride failed (cf. ref. 14). When the Gomberg reaction was carried out under anhydrous conditions, however, a 45% yield of 2-nitro-5-phenylacetophenone was attained: 4-hydroxy-6-phenylcinnoline was then available by the usual route.

For conversion of the 4-hydroxycinnolines into the parent bases a number of methods were investigated: decomposition of *N*-(6-phenyl-4-cinnolyl)-*N'*-toluene-*p*-sulphonhydrazide under a variety of conditions gave the cinnoline in an optimum overall yield of 26%; and attempt to make 6-phenyl-4-cinnolylhydrazine failed. Catalytic reduction in aqueous-alcoholic alkali (cf. ref. 15) gave only 4-ethoxy-6-phenylcinnoline. However, direct reduction of 4-hydroxycinnolines with lithium aluminium hydride was more successful: 4-hydroxycinnoline itself gave a 42% yield of cinnoline picrate which was increased to 74% by gentle oxidation of the crude product of reduction. 6- and 7-Phenylcinnoline were obtained, but in lower yields, possibly owing to the presence of more stable dihydro-compounds as intermediates which still reduced cold potassium permanganate solution after oxidation with mercuric oxide. 4-Hydroxy-3-phenylcinnoline [16] yielded by similar treatment a red, partially reduced compound which, by analogy with the red complex obtained [16] by similar reduction of 3 : 4-benzacridone, is thought to be a complex of 3-phenylcinnoline and dihydro-3-phenylcinnoline: two picrates were isolated and each gave 3-phenylcinnoline on decomposition; the possibility of picric acid's acting as an oxidising agent here may be related to the increased yields obtained when products were isolated as picrates rather than as free bases.

An attempt to prepare 8-phenylcinnoline by means of a Gomberg reaction with 8-aminocinnoline, prepared by the recorded method,[17] gave no recognisable product. Similarly, the synthesis of a 5-phenylcinnoline derivative has not yet been achieved: 2-amino-3-nitrodiphenyl was converted into the amino-nitrile but this failed to give any useful product with methylmagnesium iodide in ether or anisole. The novel method of Beech [18] for preparing methyl ketones directly from amines yielded only the deaminated product when applied to 2-amino-3-nitrodiphenyl.

Experimental

Light petroleum had b. p. 40—60° except where otherwise stated.

2-Amino-3-nitrodiphenyl.—The crude mixture (m. p. 80—90°) obtained from nitration of 2-acetamidodiphenyl (29 g.) by the method of Stepan and Hamilton [2] was added to glacial acetic acid (180 ml.) and concentrated hydrochloric acid (400 ml.) and heated under reflux for 7 hr. After cooling, the mixture was poured into an equal volume of water and made alkaline with concentrated aqueous potassium hydroxide. The brown viscous oil, obtained by extraction with benzene, was dissolved in the minimum volume of benzene and transferred to a column of alumina (200 g., type H). Elution with 1 : 5 benzene–light petroleum (700 ml.) yielded an

[11] Jones, *J. Org. Chem.*, 1945, **10**, 538.
[12] Walker and Hauser, *J. Amer. Chem. Soc.*, 1946, **68**, 1387.
[13] Simpson, Atkinson, Schofield, and Stephenson, *J.*, 1945, 646.
[14] France, Heilbron, and Hey, *J.*, 1940, 369.
[15] Stephenson, *Chem. and Ind.*, 1957, 174.
[16] Badger, Seidler, and Thomson, *J.*, 1951, 3207.
[17] Alford, Irving, Marsh, and Schofield, *J.*, 1952, 3009.
[18] Beech, *J.*, 1954, 1297.

XUM

orange oil (9·6 g.) which was further purified on a smaller column to give 2-amino-3-nitrodiphenyl as an orange solid (8·5 g., 29% yield based upon 2-acetamidodiphenyl), m. p. 50—53°.

A purer product, m. p. 53—56°, was obtained in an overall yield of 16—19% by similar chromatography of the hydrolysis product of 2-acetamido-3-nitrodiphenyl, the latter having been purified by repeated recrystallisation from benzene and aqueous alcohol.

2 : 3-*Diaminodiphenyl*.—2-Amino-3-nitrodiphenyl (2 g.) in alcohol (35 ml.) with 5% palladised charcoal (0·4 g.) was hydrogenated (5 atm.) for 2 hr. The brown oil left after removal of solvent was digested with hot light petroleum (2 × 25 ml.; b. p. 80—100°) and decanted from an insoluble tar. Evaporation of this extract to about 30 ml. furnished a pale yellow crystalline solid (1·2 g.), m. p. 86—87°, which on recrystallisation from light petroleum (b. p. 80—100°) gave very pale yellow rectangular prisms of the pure *diamine* (0·96 g., 55%), m. p. 89° (Found: C, 78·0; H, 6·6; N, 15·1. $C_{12}H_{12}N_2$ requires C, 78·2; H, 6·5; N, 15·2%).

5-*Phenylquinoxaline*.—2 : 3-Diaminodiphenyl (0·95 g.) and glyoxal sodium bisulphite (1·45 g.) in 50% alcohol (10 ml.) were stirred at 60° for 1 hr. A further portion of glyoxal sodium bisulphite (0·15 g.) was then added, and stirring at 60° continued for 2 hr. After evaporation of the alcohol, the solution was made alkaline with 6N-sodium hydroxide and extracted with ether. The dried ($MgSO_4$) extract yielded a brown solid (0·8 g.), m. p. 112—118°, which was digested with boiling light petroleum (b. p. 80—100°). The filtered digest yielded, on concentration to *ca.* 15 ml., a brown, microcrystalline solid (0·42 g., 39%), m. p. 124—124·5°, which on further recrystallisation from *n*-hexane and from aqueous methanol gave colourless needles, m. p. 124·5°, of 5-*phenylquinoxaline* (Found: C, 81·85; H, 5·0; N, 13·2. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·6%). A yellow picrate, m. p. 148°, was prepared in methanol but attempted recrystallisation led only to recovery of the base.

3 : 4-*Diaminodiphenyl*.—A solution of 4-amino-3-nitrodiphenyl (14·8 g.) in alcohol (193 ml.) was hydrogenated at 3—5 atm. for 30 min. in the presence of Adams catalyst. The filtrate was evaporated to *ca.* 40 ml., and the crude product (12·1 g., 95%), m. p. 101°, was precipitated by addition of water. 3 : 4-Diaminodiphenyl formed colourless plates, m. p. 102° (lit.,[19] m. p. 103°), from benzene–light petroleum or from dilute alcohol (Found: C, 78·2; H, 6·7; N, 15·3. Calc. for $C_{12}H_{12}N_2$: C, 78·2; H, 6·5; N, 15·2%).

6-*Phenylquinoxaline*.—3 : 4-Diaminodiphenyl (5 g.) in water (50 ml.) was treated with two portions of glyoxal sodium bisulphite (7·3 g. and 0·7 g.) as above. The cold solution was made alkaline with potassium hydroxide, and the crude material (5·6 g.), m. p. 104—106°, was powdered and extracted with boiling light petroleum, from which colourless needles (3·4 g.), m. p. 109—111°, were obtained after evaporation to about 50 ml. Successive recrystallisation from light petroleum and aqueous ethanol gave colourless needles, m. p. 112°, of 6-*phenylquinoxaline* (Found: C, 81·8; H, 4·7; N, 13·2. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·6%). A bright yellow picrate, m. p. 170° unchanged by recrystallisation from methanol, was obtained on mixing concentrated methanolic solutions of 6-phenylquinoxaline and picric acid.

2-*Acetamido*-3-*aminodiphenyl*.—2-Acetamido-3-nitrodiphenyl (3 g.) was suspended in alcohol (39 ml.) with Adams catalyst (0·1 g.) and hydrogenated at 2—5 atm. 2-*Acetamido*-3-*aminodiphenyl* formed colourless needles, m. p. 179°, from water or benzene (Found: C, 74·5; H, 6·3; N, 12·5. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2; N, 12·4%).

The Action of Acid and Alkali on 2-*Acetamido*-3-*aminodiphenyl*.—2-Acetamido-3-aminodiphenyl (1·75 g.) was boiled with concentrated hydrochloric acid (17·5 ml.) for periods of 1 to 6 hr.; glassy residues were obtained by making the solutions alkaline with 6N-sodium hydroxide, followed by chloroform-extraction. These crystallised with loss of solvent when heated on the water-bath, to form a white solid, m. p. 150—166°. Recrystallisation from aqueous ethanol gave colourless crystals, m. p. 180°, decreasing to 172° after recrystallisation from benzene–light petroleum; the higher-melting product was regained either by recrystallisation from aqueous alcohol or by drying, for 6 hr. at 110°/0·1 mm. 2-*Methyl*-7-*phenylbenzimidazole* was also obtained when 2-acetamido-3-aminodiphenyl was heated under reflux with 6N-sodium hydroxide for 2½ hr. (Found: C, 80·1; H, 5·8; N, 14·6. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8; N, 13·5%).

4-*Phenylphthalic Acid*.—Dimethyl 4-nitrophthalate (30 g.), alcohol (300 ml.), and Adams catalyst (0·3 g.) were shaken with hydrogen for 2½ hr. After filtration from the catalyst, the solution was evaporated to dryness and the residue was digested with 3N-hydrochloric acid. The filtrate was neutralised with concentrated aqueous ammonia, then extracted continuously

[19] Bell and Kenyon, *J.*, 1926, 2710.

with benzene, and the extract was evaporated to provide the amine (26 g.), m. p. 78—82°. A solution of this amine (5 g.) in glacial acetic acid (8 ml.) and benzene (15 ml.) was treated with concentrated sulphuric acid (1·5 ml.) and then stirred, at 10—15°, during the addition (in 20 min.) of freshly distilled butyl nitrite (8·5 ml.). After ¾ hr., benzene (70 ml.) was added, followed by small portions of anhydrous sodium carbonate (3·9 g.) during 1 hr. After 3 hr. the cooling-bath was removed, stirring was continued overnight, and the mixture was heated during 2 hr. to the b. p. and maintained thus for a further 2 hr. The mixture was filtered cold, the solvent removed under reduced pressure, and the semi-crystalline residue was heated with 6N-sodium hydroxide (50 ml.) under reflux for 5 hr. The ice-cooled, stirred solution was acidified with concentrated hydrochloric acid, then set aside for 1 hr., and the brown solid (3·5 g., 60%), m. p. 190—194° (decomp.), was collected, washed with water, and dried *in vacuo*.

3-*Phenylphthalic Anhydride*.—Dimethyl 3-aminophthalate (15 g.), under the conditions applied to dimethyl 4-aminophthalate above, afforded 3-phenylphthalic acid (11·1 g.), m. p. 175—177° (decomp.). The crude acid (11·8 g.) was heated with acetic anhydride (12 ml.), at 120° for 20 min., cooled, triturated with ether (2 × 20 ml.), and dried at 95°. The brown powder (8·0 g.), m. p. 143—146°, after three recrystallisations from ligroin, yielded colourless needles (5·1 g.) of the anhydride, m. p. 146—146·5° (Found: C, 74·5; H, 4·35. $C_{14}H_8O_3$ requires C, 75·0; H, 3·6%).

1 : 4-*Dihydroxy-6-phenylphthalazine*.—Crude 4-phenylphthalic acid (3·1 g.), 50% acetic acid (50 ml.), and 98—100% hydrazine hydrate (1·2 ml.) were heated under reflux for 5 hr. The solid was collected cold, washed successively with water, sodium hydrogen carbonate solution, and water, then dried at 90°. This product (2·6 g.), m. p. 307—311°, was digested with boiling acetic acid, and provided a buff-coloured solid (2·2 g.), m. p. 315°; this was sparingly soluble in the usual organic solvents, but dissolved in dilute sodium hydroxide solution after warming.

1 : 4-*Dichloro-6-phenylphthalazine*.—1 : 4-Dihydroxy-6-phenylphthalazine (1 g.) was heated with phosphorus pentachloride (approx. 3 g.) at 150—160° for 4 hr. Phosphorus oxychloride was removed at 120° under reduced pressure and the residue was extracted with boiling benzene (2 × 30 ml.). The benzene extract gave, by evaporation under reduced pressure, a waxy brown solid, easily soluble in benzene and sparingly soluble in light petroleum. From a mixture of these solvents, some red sticky solid separated; this was discarded and the liquors were evaporated to dryness. The residue was digested with boiling ligroin, cooled, filtered, and washed with light petroleum. After drying at 90°, the buff-coloured chloro-compound (0·5 g.), m. p. 150—153°, was not further purified. This product was insoluble in dilute alkali.

6-*Phenylphthalazine*.—1 : 4-Dichloro-6-phenylphthalazine (0·5 g.), m. p. 150—153°, concentrated hydriodic acid (8·5 ml.; *d* 1·94), and red phosphorus (0·4 g.) were heated under reflux for 1½ hr. The mixture was diluted with water (8·5 ml.), cooled in ice, and made alkaline with solid potassium hydroxide. The solid was collected and washed with benzene, and the washings were used (6 × 20 ml.) to extract the aqueous filtrate. The benzene extract, after being washed with water, yielded a waxy residue which formed a yellow picrate (140 mg.), m. p. 202°, from methanol; this was decomposed by 3N-sodium hydroxide (35 ml.) on the water-bath for 1½ hr. The cooled solution was extracted continuously with benzene to yield pale yellow needles (65 mg.), m. p. 137—139° (from ligroin); further recrystallisation gave colourless needles of 6-*phenylphthalazine*, m. p. 138·5—139° (Found: C, 80·9; H, 4·6. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9%).

2-*Cyano-3-nitrodiphenyl*.—2-Amino-3-nitrodiphenyl (44·8 g.) was warmed and stirred with concentrated hydrochloric acid (450 ml.) to provide the colourless hydrochloride. The mixture was stirred at 0—5° during portionwise addition of sodium nitrite (16·5 g.) in ½ hr., then for a further ½ hr. The ice-cold diazonium salt solution was led, during 1 hr., beneath the surface of a stirred cuprous cyanide solution (≯15°) to which had been added aqueous ammonia (*d* 0·880; 230 ml.) and sufficient benzene to cover the surface of the liquid (about 150 ml.). After 2 hr., the cooling-bath was removed and the mixture was stirred overnight. A benzene extract, after being washed successively with water, sodium hydroxide solution, and water, yielded an oily brown residue. This was digested repeatedly with boiling ligroin (total 1500 ml.), and the oily discoloured needles obtained on cooling were collected and washed with light petroleum. Recrystallisation from alcohol (350 ml.) yielded pale brown needles of 2-*cyano*-3-*nitrodiphenyl* (20·5 g., 44%), m. p. 130—131° (Found: C, 69·8; H, 3·4; N, 12·8. $C_{13}H_8O_2N_2$ requires C, 69·7; H, 3·6; N, 12·55%).

XUM

3-Aminodiphenyl-2-carboxyamide.—2-Cyano-3-nitrodiphenyl (1 g.) was suspended in hot alcohol (10 ml.) and added to a solution of stannous chloride (3·3 g.) in concentrated hydrochloric acid (10 ml.). The mixture was heated on the water-bath for ½ hr., cooled, made alkaline with concentrated aqueous potassium hydroxide, and extracted with ether. The oily residue afforded slightly coloured needles (210 mg., 22%), m. p. 169—170° (from benzene). Recrystallisation from water gave colourless needles of the *amide*, m. p. 171° (Found: C, 73·5; H, 5·95; N, 13·0. $C_{13}H_{12}ON_2$ requires C, 73·6; H, 5·7; N, 13·2%).

3-Amino-2-cyanodiphenyl.—A solution of 2-cyano-3-nitrodiphenyl (6 g.) in glacial acetic acid (120 ml.) was treated at 18—22° with stannous chloride–acetic anhydride reagent [20] (120 ml.), and set aside for 2 hr. The solid was collected, washed with acetic acid, and transferred to a separating funnel containing 6N-sodium hydroxide (75 ml.) and ether (75 ml.). When the solid had dissolved, the aqueous layer was extracted with ether, and the combined ether solutions were washed with water, dried ($MgSO_4$), and evaporated. Recrystallisation of the pale brown residue from ligroin gave colourless prisms of the *amino-nitrile* (3·4 g., 65%), m. p. 103—104° (Found: C, 80·4; H, 5·1; N, 14·2. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2; N, 14·4%).

3-Nitrodiphenyl-4-carboxyamide.—Finely powdered sodium nitrite (10 g.) was added during 10 min. to stirred concentrated sulphuric acid (120 ml.). The solution was cooled to 20° and powdered 4-amino-3-nitrodiphenyl (24 g.) was added during 20 min. at this temperature. After a further hour (when a drop of the solution gave no red precipitate of the amine on addition to water), the solution was poured cautiously, with stirring, into water and crushed ice (final volume *ca.* 500 ml.).

A solution of cuprous cyanide (210 ml.; prepared as usual from 87 g. of crystalline copper sulphate), aqueous ammonia (*d* 0·880; 220 ml.), and benzene (*ca.* 200 ml.) were stirred and the temperature kept below 15° by strong cooling, whilst the ice-cold diazonium salt solution was added beneath the surface during 1 hr. After being stirred for a further ½ hr., the mixture was set aside overnight. A benzene extract of the product was washed with sodium carbonate solution and with water, and evaporated, yielding a brown oil which was mixed with " Hyflo " and extracted with *n*-hexane (300 ml.) in a Soxhlet apparatus. The brown product which crystallised on cooling (11·2 g.; m. p. 110—116°) was collected, air-dried, and recrystallised from ethanol, giving discoloured needles (10·3 g., 41%), m. p. 117—119°. A solution of this nitro-nitrile (3·5 g.) in acetone (100 ml.) and N-sodium hydroxide (50 ml.) was treated with 100-vol. hydrogen peroxide (30 ml.). The solution was warmed gently for 1½ hr., then heated under reflux for ½ hr., the acetone was distilled off, and, from the cooled residue, after dilution with water (150 ml.), a pale brown solid (3·67 g., 97%), m. p. 192—193°, was collected. Recrystallisation from aqueous alcohol and from benzene afforded colourless needles of the *nitro-amide*, m. p. 195° (Found: C, 64·25; H, 4·0; N, 10·3. $C_{13}H_{10}O_3N_2$ requires C, 64·45; H, 4·2; N, 11·6%).

3-Nitrodiphenyl-4-carboxylic Acid.—The last-mentioned amide (18·5 g.; m. p. 191—192°), in acetic acid (300 ml.), water (164 ml.), and concentrated sulphuric acid (212 ml.), was stirred at 5—10° during portionwise addition (20 min.) of sodium nitrite (10·3 g.), and for a further 1½ hr. The solution was set aside overnight and diluted to *ca.* 1 l., and the brown solid (18·3 g.), m. p. 200—203°, was reprecipitated from N-sodium carbonate with concentrated hydrochloric acid. Recrystallisation from aqueous alcohol gave colourless needles of the *acid*, m. p. 205° (Found: C, 64·5; H, 4·3; N, 5·4. $C_{13}H_9O_4N$ requires C, 64·2; H, 3·7; N, 5·8%).

4-Acetyl-3-nitrodiphenyl.—The foregoing acid (17 g.) and thionyl chloride (56 ml.) were heated under reflux for ½ hr. The excess of thionyl chloride was removed on the water-bath, finally under reduced pressure, and the brown residue was warmed with dry ether (70 ml.) and filtered. The pale yellow solution of the acid chloride was used directly as described below.

To a mixture of magnesium turnings (1·9 g.), absolute ethanol (1·75 ml.) and carbon tetrachloride (0·4 ml.), were added sodium-dried ether (52·5 ml.), and then diethyl malonate (12·3 g.) and absolute ethanol (7 ml.) in sodium-dried ether (9·1 ml.), at a rate sufficient to maintain boiling. Heating under reflux was continued for 3 hr. and an ethereal solution of the acid chloride was added in 15 min. with stirring. After 2½ hours' boiling, the white viscous gum was cooled and a solution of concentrated sulphuric acid (5 ml.) in water (70 ml.) was added. The aqueous layer was extracted once with ether, and the combined extracts were evaporated to dryness; the residue was heated under reflux with acetic acid (21 ml.), water (14 ml.), and

[20] Albert and Linnell, *J.*, 1936, 1617.

concentrated sulphuric acid (2·6 ml.) for 10 hr. After dilution with an equal volume of water and cooling, the oily solid was collected and dried *in vacuo*. The crude product yielded, by digestion with small portions of boiling light petroleum (b. p. 60—80°; 650 ml.), yellow needles (12·8 g.), m. p. 75—79°, which, on further recrystallisation from light petroleum (b. p. 80—100°) and from *n*-hexane, gave colourless needles of the *nitro-ketone*, m. p. 79·5° (Found: C, 69·95; H, 4·85; N, 5·15. $C_{14}H_{11}O_3N$ requires C, 69·7; H, 4·6; N, 5·8%).

4-*Acetyl*-3-*aminodiphenyl*.—4-Acetyl-3-nitrodiphenyl (7·3 g.) was dissolved in glacial acetic acid (60 ml.), and the stannous chloride–acetic anhydride reagent [20] (170 ml.) was added fairly rapidly at <22°. After 4 hr., working up as for 3-amino-2-cyanodiphenyl (above) yielded a yellow residue, m. p. 109—114°. Two recrystallisations from *n*-hexane gave colourless needles (4·7 g., 73%), m. p. 119·5°, of the *amino-ketone* (Found: C, 79·1; H, 4·9; N, 7·5. $C_{14}H_{13}ON$ requires C, 79·6; H, 6·2; N, 6·6%).

4-*Hydroxy*-7-*phenylcinnoline*.—Powdered 4-acetyl-2-aminodiphenyl (2·25 g.) was stirred with concentrated hydrochloric acid (75 ml.) until dissolved and then diazotised in the usual way. The solution was stirred at 55—60° for 3½ hr. (by which time it no longer coupled with alkaline β-naphthol), diluted with about twice its volume of water, cooled, and filtered. The dark residue was extracted with hot 3N-sodium hydroxide which yielded on acidification a white solid (1·14 g.), m. p. 312—316°. This dissolved slowly in boiling alcohol and concentration of the solution gave colourless needles of the *hydroxycinnoline* (0·88 g., 37%), m. p. 323—325° (unchanged by recrystallisation from methanol or acetic acid) (Found: C, 75·9; H, 4·7; N, 11·6. $C_{14}H_{10}ON_2$ requires C, 75·65; H, 4·5; N, 12·6%).

3-*Acetyl*-4-*nitrodiphenyl*.—5-Amino-2-nitroacetophenone [13] (15 g.) was dissolved in warm glacial acetic acid (45 ml.), concentrated sulphuric acid (5 ml.) and benzene (50 ml.) were added, and the solution was stirred at 15° during addition of butyl nitrite (13·5 ml.) in 15 min. Benzene (250 ml.) was added, the mixture was stirred for ½ hr., and anhydrous sodium carbonate (10 g.) was added in small portions during ¾ hr. After 3 hours' stirring at 15°, the cooling-bath was removed and stirring was continued overnight. A yellow, thermally unstable solid was collected and washed with benzene, and the filtrate washed successively with dilute sodium hydroxide (3×) and finally with water. The dried ($MgSO_4$) extract was evaporated to dryness on the water-bath, finally at reduced pressure to remove butyl acetate. The oily brown residue was transferred in benzene (30 ml.) and light petroleum (*ca.* 15 ml.) to a column of alumina (150 g., type H), which was eluted with 2 : 3 benzene–light petroleum. Evaporation of the coloured eluate (1 l.) and recrystallisation of the residue from light petroleum (b. p. 60—80°) gave pale yellow needles of 3-*acetyl*-4-*nitrodiphenyl* (8·1 g., 45%), m. p. 86° (Found: C, 68·9; H, 4·5; N, 5·45. $C_{14}H_{11}O_3N$ requires C, 69·6; H, 4·6; N, 5·8%).

4-*Hydroxy*-6-*phenylcinnoline*.—The stannous chloride–acetic anhydride reagent (375 ml.) was stirred below 25° during portionwise addition of 3-acetyl-4-nitrodiphenyl (15 g.) and then set aside at room temperature for 4 hr. The mixture was worked up as usual and yielded from *n*-hexane pale yellow prisms (11·0 g.), m. p. 80—84°.

This crude, finely powdered amine was stirred with concentrated hydrochloric acid (350 ml.) and treated at 0—5° with a saturated solution of sodium nitrite (4·05 g.). After a further ½ hr. at this temperature, the solution was stirred at 55—60° until it no longer coupled with alkaline β-naphthol (4 hr.), diluted with twice its volume of water, and allowed to cool. The solid was extracted with hot 3N-sodium hydroxide, from which the crude *hydroxycinnoline* (7·0 g.), m. p. 282—288°, was obtained by acidification with concentrated hydrochloric acid. It separated from alcohol as colourless needles (5·3 g., 38% overall), m. p. 292—295° raised to 294—296° by further recrystallisation (Found: C, 74·7; H, 4·6; N, 12·1. $C_{14}H_{10}ON_2$ requires C, 75·6; H, 4·5; N, 12·6%).

4-*Chloro*-6-*phenylcinnoline*.—4-Hydroxy-6-phenylcinnoline (3·9 g.; m. p. 292—295°) and phosphorus oxychloride (40 ml.) were heated under reflux for 15 min., cooled, and added slowly to 6N-sodium hydroxide (100 ml.) and crushed ice. Recrystallisation of solid (4·1 g.), m. p. 146—148°, from ligroin gave pale yellow needles of the *chloro-compound* (3·75 g., 89%), m. p. 150—152° raised to 151—152° on further recrystallisation (Found: C, 70·2; H, 3·8; N, 11·5; Cl, 14·4. $C_{14}H_9N_2Cl$ requires C, 69·85; H, 3·8; N, 11·6; Cl, 14·75%).

4-*Chloro*-7-*phenylcinnoline*.—4-Hydroxy-7-phenylcinnoline (250 mg., m. p. 232—235°) and phosphorus oxychloride (3 ml.), under the conditions used for the 6-phenyl isomer, yielded a green solid (230 mg.; m. p. 105—108°), which on recrystallisation from ligroin or light petroleum gave pale yellow plates of the *chloro-compound* (150 mg., 55%), m. p. 124—125°

(Found: C, 68·8; H, 3·8; N, 11·8; Cl, 15·0. $C_{14}H_9N_2Cl$ requires C, 69·95; H, 3·8; N, 11·6; Cl, 14·75%).

Reduction of 4-*Hydroxycinnoline.*—4-Hydroxycinnoline (500 mg.) was heated under reflux in tetrahydrofuran (10 ml.) with lithium aluminium hydride (270 mg.) for 8 hr. Next day, benzene (30 ml.) was added, the complex was decomposed by water, and inorganic material was filtered off. The benzene layer was evaporated to 10 ml. and heated under reflux with an excess of red mercuric oxide for 3 hr. Evaporation of the filtrate to dryness and treatment with methanolic picric acid gave cinnoline picrate (900 mg.), m. p. 190—194°.

6-*Phenylcinnoline.*—4-Hydroxy-6-phenylcinnoline (300 mg.) was heated under reflux in tetrahydrofuran (6 ml.) with lithium aluminium hydride (140 mg.) for 15 hr. By the above procedure, an oily residue was obtained, which, on recrystallisation from ligroin, gave a yellow solid (110 mg.), m. p. 102—106°. Five recrystallisations from ligroin gave pale yellow needles, m. p. 111—111·5°, which readily formed a picrate, m. p. 176°. The same picrate was obtained by boiling the crude reduction product (m. p. 102—106°) with picric acid in methanol solution. Recrystallisation from alcohol or benzene gave deep yellow needles of 6-*phenylcinnoline picrate*, m. p. 176° (Found: C, 55·2; H, 3·1; N, 14·8. $C_{20}H_{13}O_7N_5$ requires C, 55·2; H, 3·0; N, 16·1%).

7-*Phenylcinnoline.*—4-Hydroxy-7-phenylcinnoline (150 mg.), tetrahydrofuran (3 ml.), and lithium aluminium hydride (70 mg.), by the above procedure, yielded an oily residue, which was dissolved in the minimum volume of methanol and boiled with methanolic picric acid for 10 min. The somewhat gummy picrate separated from methanol as brown needles (140 mg., 48%), m. p. 175·5—177° unchanged by recrystallisation from aqueous alcohol or benzene.

In a similar experiment, 380 mg. of the hydroxycinnoline provided a yellow solid (100 mg.; m. p. 103—106°) by extraction of the crude reduction product with 5N-hydrochloric acid. Five recrystallisations from aqueous alcohol gave very pale yellow needles of 7-*phenylcinnoline*, m. p. 116° (Found: C, 80·8; H, 5·1; N, 12·7. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·5%). This compound gave the same picrate (m. p. 177°) as was obtained in the previous experiment.

Reduction of 4-*Hydroxy*-3-*phenylcinnoline.*—4-Hydroxy-3-phenylcinnoline (5 g.), tetrahydrofuran (100 ml.), and lithium aluminium hydride (2·5 g.) were heated under reflux for 16 hr. After decomposition of the complex, as before, the residue was boiled with red mercuric oxide (15 g.) in benzene (75 ml.) for 4½ hr. Filtration and evaporation yielded a sticky solid, which gave red needles (1·0 g.), m. p. 119—120°, after several recrystallisations from *n*-hexane and from aqueous alcohol (Found: C, 80·8; H, 4·9; N, 13·7. $C_{28}H_{22}N_4$ requires C, 81·1; H, 5·3; N, 13·5%). An acetone solution of this compound decolorised 0·1% potassium permanganate solution in the cold. A yellow picrate, m. p. 150—151°, was prepared in methanol.

The residue obtained by evaporation of the hexane mother-liquors was boiled with picric acid in methanol, whereby a mixture of picrates (1·8 g.; 148—151°) was obtained. Recrystallisation from alcohol and benzene gave green needles (1·2 g.), m. p. 151°, not depressed on admixture with the picrate obtained from the red compound above; a yellow picrate, m. p. 157°, was also obtained from the mixture. Each of these picrates was decomposed by heating it for 20 min. with 4N-sodium hydroxide, to yield the same product which crystallised in yellow needles, m. p. 118—119°, from ligroin, differing from the red compound, m. p. 119—120°, and not decolorising potassium permanganate solution. With methanolic picric acid, the green 3-*phenylcinnoline picrate*, m. p. 151°, was regenerated (Found: C, 54·3; H, 3·2; N, 15·45. $C_{20}H_{13}O_7N_5$ requires C, 55·2; H, 3·0; N, 16·1%).

4-*Ethoxy*-6-*phenylcinnoline.*—This was obtained during attempted hydrogenolysis of 4-chloro-6-phenylcinnoline in 0·4N-aqueous-alcoholic sodium hydroxide. The *derivative* separated as colourless needles, m. p. 176°, from ligroin or aqueous alcohol (Found: C, 76·1; H, 5·4; N, 10·7. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6; N, 11·2%). This product formed a picrate, m. p. 168°, in methanol.

The authors are indebted to Messrs. Albright and Wilson Ltd. for a grant (to C. J. S.).

CHEMISTRY DEPARTMENT, CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.3.
DERBY AND DISTRICT COLLEGE OF TECHNOLOGY.
[*Received, December 5th,* 1958.]

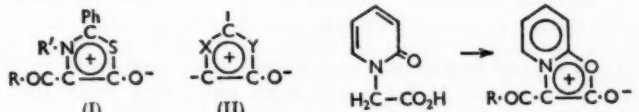
574. *Some New Mesoionic Compounds.*

By Alexander Lawson and D. H. Miles.

Mesoionic compounds belonging to the systems [II; X = N, Y = S; X = N, Y = O; X = N (of pyridine), Y = N; X = N, Y = NPh] have been prepared from *N*-substituted thiobenzoylglycines, 1,2-dihydro-2-oxo-1-pyridylacetic acid, *N*-substituted *N*-2-pyridylglycines, and *N*-(*N*-phenylbenzimidoyl)aminoacetic acids respectively. Some of their properties are described.

Lawson and Searle [1] treated *N*-alkyl-*N*-thiobenzamido-acids with acid anhydrides and obtained products formulated as mesoionic compounds (I; R = Me, Et, R′ = Me, Et). In continuation of this work [2] the general system (II) has been studied, the hetero-atoms or -groups being varied: X = N, Y = S; X = N, Y = O; X = N (of pyridine), Y = N; X = N, Y = NPh. Mesoionic compounds corresponding to each of these systems have been prepared and their general properties and ultraviolet spectra recorded. The formulation adopted is that put forward by Baker and Ollis.[3,4] The tautomeric forms possible are restricted to those in which the cyclic carbonyl group is totally polarised, in order that the six π-electrons required for the ring to assume an aromatic character are to be available. However, infrared spectroscopic data [1] show that for anhydro-(4-acetyl-5-hydroxy-3-methyl-2-phenylthiazolium hydroxide) (I; R = R′ = Me) this is only partially justified.

Katritzky's nomenclature [5] has been adopted in this communication.



(I) (II) (III) (IV)

The range of compounds of the type (I) was extended by the preparation of the *N*-phenyl and the *C*-benzoyl derivative (I; R = Me, Ph; R′ = Me, Ph). Thiobenzoyl-*N*-phenylglycine cyclised very readily when warmed with acid anhydrides. Ring-closure with *C*-benzoylation was achieved by heating the acid with benzoyl chloride and pyridine or with benzoic anhydride. The properties of these compounds were very similar to those of the analogues prepared by Lawson and Searle.[1] The compounds from *N*-phenylglycine were obtained in greater yield and under milder dehydrating conditions than those from sarcosine. It had been expected that the increased potentiality of charge distribution provided by the phenyl substituent would stabilise the mesoionic compound.

1,2-Dihydro-2-oxo-1-pyridylacetic acid [6] (III) was prepared by the action of chloroacetic acid upon 2-pyridone and elimination of hydrochloric acid by heat. With acid anhydrides it gave crystalline, neutral mesoionic compounds (IV; R = Me, Et). Hydrolysis of these with dilute acid yielded a syrup from which 2-pyridone was isolated; the compounds were also decomposed by boiling water, to carbon dioxide and an intractable syrup.

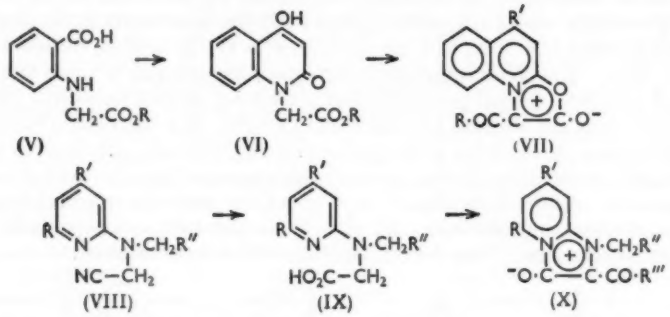
Attempts to prepare the analogous quinoline derivative (VII; R = Me, R′ = H) were unsuccessful owing to failure to obtain the intermediate acetic acid. However, the action of acetic anhydride and 3-picoline on phenylglycine-*o*-carboxylic acid (V; R = H) yielded a compound $C_{21}H_{18}O_5N_2$. This, if formulated as $C_{15}H_{11}O_5N,C_6H_7N$, would correspond to the required mesoionic compound (VII; R = Me, R′ = OAc) incorporating picoline.

[1] Lawson and Searle, *J.*, 1957, 1556.
[2] Lawson and Miles, *Chem. and Ind.*, 1958, 461.
[3] Baker and Ollis, *Quart. Rev.*, 1957, **11**, 15.
[4] Baker, *Proc. Chem. Soc.*, 1959, 75.
[5] Katritzky, *Chem. and Ind.*, 1955, 521.
[6] Kirpal, *Ber.*, 1924, **57**, 1954.

XUM

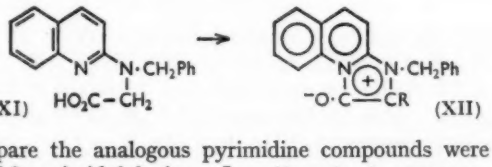
All attempts to remove picoline from the compound were unsuccessful. Treatment of phenylglycine-*o*-carboxylic acid with acetic anhydride and other tertiary amines led to charring and tar formation. Proof of the structure of this compound awaits further investigation.

Compounds of the type (X; R = H or Me, R′ = H or Me, R″ = Me or Ph, R‴ = Me or Et) were prepared by the action of acid anhydrides upon *N*-alkyl- or *N*-alkylaryl-substituted *N*-2-pyridylglycines (IX; R = H or Me, R′ = H or Me, R″ = Me or Ph). These compounds were prepared by hydrolysis of the corresponding nitriles (VIII; R = H or Me, R′ = H or Me, R″ = Me or Ph), obtained by the action of sodium hydrogen sulphite, formaldehyde, and sodium cyanide on 2-aminopyridines,[7] followed by benzylation or ethylation of the product and ring-closure. The mesoionic compounds were yellow and



crystalline, and had a green fluorescence in solution. They were unusual in being readily soluble without decomposition in hot water, from which they crystallised on cooling. Unlike compounds of type (I), they were not attacked by hot benzylamine or aniline,[1] or by hot alkali or acid. Similar compounds were obtained from 2-amino-4-methyl- and -4,6-dimethyl-pyridine.

N-Benzyl-*N*-2-quinolylglycine (XI) was produced by a route similar to that used for the pyridyl-acid. The solution obtained on hydrolysis of the corresponding nitrile possessed a yellow-green fluorescence and a small amount of benzene-soluble, neutral material was extracted from it. This was the unacylated mesoionic compound (XII; R = H) which was also obtained as a by-product of the action of acetic anhydride on the acid, the major yield being the acylated mesoionic compound (XII; R = Ac). Prolonged action of boiling dilute hydrochloric acid on the amino-acid also yielded the unacylated compound. This system, of those examined, appears to be unique in giving ring-closure under acid conditions without the need for reaction with acid anhydrides. This behaviour is doubtless associated with the facility of charge distribution in a system with such a high degree of conjugation. These mesoionic compounds of the type (II; X = N, Y = N) are reminiscent of those prepared by Bristow *et al.*[5]

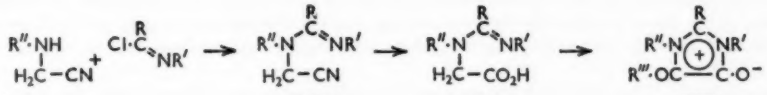


Attempts to prepare the analogous pyrimidine compounds were frustrated by the inaccessibility of *N*-2-pyrimidylglycine. In attempts to prepare this intermediate, 2-aminopyrimidine was treated with bromoacetic ester. An intense purple colour was developed, and the pigment present could be conveniently isolated by chromatography.

[7] Bristow, Charleton, Peak, and Short, *J.*, 1954, 621.

It was tinctorially strong, but light-sensitive and thus unsuitable as a dye. The structure of the compound was not elucidated.

Compounds of type (XV; R = R′ = Ph, R″ = R‴ = Me) were prepared by ring closure of *N*-(*N*-phenylbenzimidoyl)amino-acids (XIV; R = R′ = Ph, R″ = Me). *N*-Phenylbenzimidoyl chloride with methylaminoacetonitrile in the presence of triethylamine yielded *N*-methyl-*N*-(*N*-phenylbenzimidoyl)aminoacetonitrile (XIII; R = R′ = Ph, R″ = Me) from which the amino-acid was obtained by hydrolysis with hydrochloric acid. Warming this amino-acid with acid anhydrides afforded a purple fluorescence and the product was obtained as white crystals. These compounds were remarkably stable, being unreactive towards hot acids, alkalis, and benzylamine. They melted without decomposition above 200°, and crystallised from water, in which they were sparingly soluble.



(XIII) (XIV) (XV)

The ultraviolet spectra of our new mesoionic compounds were all qualitatively similar. The acetyl derivatives had somewhat higher extinction coefficients than the propionyl derivatives. Strong absorption was noted in all cases at ~2600 Å, presumably resulting from the imposition of the bathochromic shift upon the basic aromatic character of the mesoionic ring systems.

In accordance with Searle and Lawson's observations that the carbonyl group in compounds of type (I) is highly polarised, it proved impossible to prepare ketonic derivatives (such as 2,4-dinitrophenylhydrazones) from any of the compounds described. They did not form picrates or salts with mineral acids.

Experimental

N-Phenyl-N-thiobenzoylglycine Ethyl Ester.—*N*-Phenylglycine ethyl ester (10 g.) and benzoic anhydride (26 g., 2·1 mol.) were refluxed in benzene (75 ml.) for 6 hr. The solvent was removed under reduced pressure and the resultant syrup washed with sodium hydrogen carbonate solution. Repeated crystallisation from aqueous alcohol gave *N*-benzoyl-*N*-phenylglycine ethyl ester, m. p. 64° (7 g., 45%). This ester (5 g.) and phosphorus pentasulphide (5 g.) were refluxed for 2 hr. in benzene (50 ml.). The yellow filtrate was evaporated under reduced pressure and the resultant oil continuously extracted with light petroleum (b. p. 40—60°). After concentration and cooling, the material obtained was recrystallised from light petroleum to give *N-phenyl-N-thiobenzoylglycine ethyl ester* (2·25 g., 42%), yellow needles, m. p. 88—89° (Found: C, 68·2; H, 5·7. $C_{17}H_{17}O_2NS$ requires C, 68·4; H, 5·5%).

N-Phenyl-N-thiobenzoylglycine.—The above ester (1 g.) was dissolved in a solution of potassium hydroxide (0·19 g., 1 mol.) in ethanol (25 ml.) and kept for 4 days at room temperature. After removal of the solvent under reduced pressure, the resulting solid was dissolved in water, and *N-phenyl-N-thiobenzoylglycine* (0·8 g., 87%) precipitated by addition of acid. Recrystallisation from aqueous ethanol gave yellow prisms (0·7 g., 76%), m. p. 180—182° (Found: C, 66·5; H, 4·7. $C_{15}H_{13}O_2NS$ requires C, 66·4; H, 4·8%).

Ring-closure of N-Phenyl-N-thiobenzoylglycine.—*N*-Phenyl-*N*-thiobenzoylglycine (0·5 g.) was heated with acetic anhydride (10 ml.) for 0·5 hr. The solution rapidly darkened and the acetic anhydride was removed by evaporation under reduced pressure and by two subsequent evaporations with xylene. Two crystallisations from benzene–light petroleum (b. p. 40—60°) gave *anhydro-(4-acetyl-5-hydroxy-2,3-diphenylthiazolium hydroxide)* (0·3 g., 63·3%), yellow prisms, m. p. 170—172° (Found: C, 68·8; H, 4·2. $C_{17}H_{13}O_2NS$ requires C, 69·1; H, 4·4%), $\lambda_{max.}$ 2420, 2780 Å in ethanol (ε 7880, 9550).

Ring-closure, with C-Benzoylation, of Thiobenzoylsarcosine.—(*a*) Thiobenzoylsarcosine [1] (1 g.) was heated on the water-bath with benzoic anhydride (1·6 g., 1·5 mol.) for 2 hr., the product being dissolved in methanol and refluxed for 2 hr. All the volatile components were

XUM

evaporated at 12 mm. on the steam-bath, and the residual solid was extracted with benzene. Concentration gave *anhydro*-(4-*benzoyl*-5-*hydroxy*-3-*methyl*-2-*phenylthiazolium hydroxide*) (0·3 g.), pale yellow needles, m. p. 220—221° (Found: C, 68·7; H, 4·1; S, 10·4. $C_{17}H_{13}O_2NS$ requires C, 69·1; H, 4·4; S, 10·85%), $\lambda_{max.}$ 2400, 2460, 2550 Å in ethanol (ε 11,590, 11,180, 10,680). (*b*) To thiobenzoylsarcosine (1 g.) in pyridine (5 ml.) benzoyl chloride (4 ml.) was added slowly with cooling. The dark brown solution was warmed to 45—50° for 15 min., then evaporated under reduced pressure, and the residue washed with dilute hydrochloric acid and water. The semi-solid residue was crystallised from benzene–light petroleum (b. p. 40—60°) and then from benzene, to yield the mesoionic compound (0·5 g.), m. p. 220°.

1,2-*Dihydro*-2-*oxo*-1-*pyridylglycine*.—2-Pyridone (2 g., 1 mol.) and chloroacetic acid (2 g., 1 mol.) were dissolved in ethanol (20 ml.) and warmed to 65° for 0·5 hr. After cooling, recrystallisation from ethanol gave 1-carboxymethyl-2-hydroxypyridinium hydrochloride (3·3 g., 82·5%), felted needles, m. p. 96—98°. This salt (2 g.) was heated at 170—180° (paraffin-wax bath) for 1·5 hr., by which time evolution of hydrochloric acid was complete. An ethanolic solution of the brown solid obtained on cooling was decolorised with charcoal, and on concentration and cooling to −10°, the pyridone-acid separated as needles, m. p. 215—218° (0·8 g., 49%).

Ring-closure.—The acid (0·5 g.) was heated with acetic anhydride (5 ml.) for 2 hr. on the steam-bath. The straw-coloured solution was evaporated under reduced pressure, and traces of acetic anhydride were removed by adding, and evaporating under reduced pressure, two 10 ml. portions of xylene. The residual solid, crystallised from benzene–light petroleum (b. p. 40—60°), yielded *anhydro*-[4-*acetyl*-5-*hydroxypyridino*(2′,1′-2,3)*oxazolium hydroxide*] (IV; R = Me) (0·3 g., 51·6%), felted needles, m. p. 170—171° (Found: C, 60·9; H, 3·95; N, 7·9. $C_9H_7O_3N$ requires C, 61·0; H, 3·95; N, 7·9%), $\lambda_{max.}$ 2425, 2550, 2900, 3350 Å in ethanol (ε 19,426, 16,000, 5760, 14,300).

The homologous 4-*propionyl derivative*, m. p. 146—147·5°, silvery leaflets from benzene (55%), was obtained by treating the pyridone-acid with propionic anhydride (Found: C, 62·6; H, 4·7; N, 7·0. $C_{10}H_9O_3N$ requires C, 62·8; H, 4·7; N, 7·3%), $\lambda_{max.}$ 2425, 2550, 2900, 3350 Å in ethanol (ε 13,820, 10,470, 3035, 10,180).

Reactions.—(*a*) The compound (IV; R = Me) (0·1 g.) in boiling water evolved carbon dioxide (approx. 0·5 mol.). Evaporation under reduced pressure then yielded a tar. (*b*) The compound (0·1 g.) was refluxed in benzylamine (5 ml.) for 1 hr. Addition of ligroin to the cooled solution precipitated a yellow oil which solidified on scratching. Crystallisation from benzene–light petroleum (b. p. 40—60°) and then from acetone gave felted needles (0·1 g.), m. p. 199—200° (Found: C, 69·0; H, 5·6; N, 11·5. $C_{14}H_{14}O_2N_2$ requires C, 69·0; H, 5·8; N, 11·5%).

Ring-closure of Phenylglycine-o-carboxylic Acid.—To phenylglycine-*o*-carboxylic acid (5 g.) in acetic anhydride (40 ml.), picoline (10 ml.) was added cautiously and with cooling. The dark brown solution, after 1 hr. at room temperature, was refluxed for 1·5 hr. The volatile components were removed under reduced pressure and the resultant tar extracted with light petroleum (b. p. 60—80°). On decolorisation with charcoal and concentration, long colourless needles, m. p. 80—83°, separated (0·9 g.) (Found: C, 66·7; H, 4·8; N, 7·0. $C_{15}H_{11}O_5N,C_6H_7N$ requires C, 66·7; H, 4·8; N, 7·0%). Refluxing this material with water or dilute hydrochloric acid gave unresolvable tars, while small quantities of carbon dioxide were evolved. No evidence of the liberation of picoline was obtained.

Ring-closure of N-*Benzyl*-N-2-*pyridylglycine*.—*N*-Benzyl-*N*-2-pyridylaminoacetonitrile [5] (9 g.) was heated with 5N-hydrochloric acid (50 ml.) for 1 hr, The solution was made alkaline with 3N-sodium hydroxide and evaporated to dryness under reduced pressure. The residue was extracted with ethanol, ether was added, and the solution kept at −10° for 24 hr.; sodium *N*-benzyl-*N*-2-pyridylglycine, m. p. 300—301°, crystallised (6·5 g., 58%).

Sodium *N*-benzyl-*N*-2-pyridylglycine (5 g.) was heated on the water-bath with acetic anhydride (50 ml.) for 1 hr. The solution rapidly became yellow with a slight green fluorescence and eventually became dark green. Evaporation under reduced pressure and then twice more with 10 ml. portions of xylene gave an oil which was extracted with benzene and decolorised with charcoal. Concentration of the solution and addition of light petroleum (b. p. 40—60°) provided *anhydro*-[4-*acetyl*-3-*benzyl*-5-*hydroxypyridino*(1′,2′-1,2)*imidazolium hydroxide*] (X; R = R′ = H, R″ = Ph, R‴ = Me), yellow needles, m. p. 170—171° (3·5 g.) (Found: C, 72·1; H, 5·3. $C_{16}H_{14}O_2N_2$ requires C, 72·1; H, 5·3%), $\lambda_{max.}$ 2620 Å in ethanol (ε 15,045).

N-Benzyl-*N*-2-pyridylglycine with propionic anhydride similarly gave the *propionyl analogue*,

XUM

yellow needles (80%), m. p. 116—117°, $\lambda_{max.}$ 2620 Å in ethanol (ε 14,950) (Found: C, 72·5; H, 5·7. $C_{17}H_{16}O_2N_2$ requires C, 72·9; H, 5·7%).

Ring-closure of N-*Ethyl*-N-2-*pyridylglycine*.—*N*-Ethyl-*N*-2-pyridylaminoacetonitrile was hydrolysed as in the case of the benzyl derivative. The amino-acid and the sodium salt proved difficult to crystallise and the residue, obtained by evaporation under reduced pressure, of the basified hydrolysate, was treated directly with acetic anhydride. *Anhydro*-[4-*acetyl*-3-*ethyl*-5-*hydroxypyridino*(1′,2′-1,2)*imidazolium hydroxide*] (X; R = R′ = H, R″ = R‴ = Me), m. p. 195—197°, crystallised from benzene as yellow prisms (49%) (Found: C, 64·6; H, 6·0; N, 14·0. $C_{11}H_{12}O_2N_2$ requires C, 64·6; H, 5·9; N, 13·7%), $\lambda_{max.}$ 2620, 4000 Å in ethanol (ε 13,810, 9085).

A *propionyl homologue*, obtained by treating the amino-acid with propionic anhydride, crystallised as yellow prisms (61%), m. p. 150—151° (Found: C, 65·8; H, 6·5. $C_{12}H_{14}O_2N_2$ requires C, 66·0; H, 6·4%).

The 4-*benzoyl homologue*, yellow prisms (from benzene), m. p. 185° (40%), was similarly prepared by the action of benzoyl chloride–pyridine on the amino-acid (Found: C, 71·8; H, 5·55. $C_{16}H_{14}O_2N_2$ requires C, 72·1; H, 5·3%).

N-*Benzyl*-N-(4-*methyl*-2-*pyridyl*)*glycine*.—*N*-(4-Methyl-2-pyridyl)aminoacetonitrile was prepared by a modification of the method of Bristow *et al.*[7] 40% Aqueous formaldehyde (10·5 ml.) and 38% sodium hydrogen sulphite solution (27·2 ml., 1·5 mol.) were mixed and heated to 95° for 0·5 hr. 2-Amino-4-methylpyridine (14·1 g.), in 50% aqueous alcohol (100 ml.), was added to the mixture and the whole was refluxed with stirring for 2 hr. The solution was cooled and sodium cyanide (13·1 g.) in water (26 ml.) added slowly, an exothermic reaction resulting. The solution was refluxed with stirring for 20 hr. and the solvents were evaporated under reduced pressure. The solid was extracted with chloroform (500 ml.), and the volume of the extract reduced to 50 ml. On cooling, the product separated as brown nodules. Recrystallisation from ethyl acetate gave N-(4-*methyl*-2-*pyridyl*)*aminoacetonitrile*, prisms (12·1 g., 88·8%), m. p. 116—117° (Found: C, 65·0; H, 6·1. $C_8H_9N_3$ requires C, 65·3; H, 6·1%).

This nitrile (5 g.) in benzene (50 ml.) was refluxed with benzyl chloride (10 ml.) for 15 min. On cooling, the N-*benzyl*-N-(4-*methyl*-2-*pyridyl*)*aminoacetonitrile hydrochloride* separated; it recrystallised from ethanol as prisms (4·3 g., 53%), m. p. 265° (decomp.) (Found: C, 65·9; H, 6·1. $C_{15}H_{15}N_3$,HCl requires C, 66·0; H, 6·1%).

The hydrochloride (3 g.) was hydrolysed to the acid as in the case of *N*-benzyl-*N*-2-pyridylglycine. The sodium salt of the amino-acid did not crystallise from the ethanolic solution and was precipitated with dry ether as an amorphous solid (3 g.), m. p. 270—280°.

Ring-closure of N-*Benzyl*-N-(4-*methyl*-2-*pyridyl*)*glycine*.—The sodium salt (1·5 g.) was heated with acetic anhydride (10 ml.) on the water-bath for 0·5 hr., then treated as above. Crystallisation from benzene gave *anhydro*-[4-*acetyl*-3-*benzyl*-5-*hydroxy*-4′-*methylpyridino*-(1′,2′-1,2)*imidazolium hydroxide*], yellow prisms exhibiting a yellow-green fluorescence in solution (1·1 g., 67%) (Found: C, 73·0; H, 5·6. $C_{17}H_{16}O_2N_2$ requires C, 72·9; H, 5·7%).

Ring-closure of N-*Ethyl*-N-(4-*methyl*-2-*pyridyl*)*glycine*.—*N*-(4-Methyl-2-pyridyl)aminoacetonitrile (5 g.) was warmed for 0·5 hr. with ethyl iodide (5 g.) in dry benzene (20 ml.), the product separating on cooling as pale yellow prisms. Recrystallisation from ethanol gave *N*-ethyl-*N*-(4-methyl-2-pyridyl)aminoacetonitrile hydriodide (4·9 g., 48·2%), m. p. 185° (Found: C, 39·7; H, 4·6. $C_9H_{11}N_3$,HI requires C, 39·6; H, 4·6%).

Hydrolysis, as previously, gave an uncrystallisable product, which, warmed with acetic anhydride on the water bath for 0·5 hr., gave *anhydro*-[4-*acetyl*-3-*ethyl*-5-*hydroxy*-4′-*methylpyridino*(1′,2′-1,2)-*imidazolium hydroxide*], yellow prisms (from benzene) (42%), m. p. 209° (Found: C, 66·6; H, 6·35. $C_{12}H_{14}O_2N_2$ requires C, 66·2; H, 6·4%).

Ring-closure of N-*Benzyl*-N-(4,6-*dimethyl*-2-*pyridyl*)*glycine*.—The nitrile, prepared as above, crystallised from chloroform–light petroleum (b. p. 40—60°) as prisms (97%), m. p. 92° (Found: C, 67·2; H, 7·0. $C_9H_{11}N_3$ requires C, 67·1; H, 6·8%). The *benzyl derivative hydrochloride*, prepared as above, crystallised from ethanol–ether as prisms (41·4%), m. p. 238—240° (Found: C, 66·2; H, 6·0. $C_{16}H_{17}N_3$,HCl requires C, 66·6; H, 6·25%).

Hydrolysis was effected as previously and the acid hydrolysate made alkaline with sodium hydroxide and evaporated to dryness. The residue on treatment with acetic anhydride on the steam-bath developed a red-green fluorescence, assuming in 2 hours a blue-brown colour. The solution, processed as previously, gave *anhydro*-[4-*acetyl*-3-*benzyl*-5-*hydroxy*-4′,6′-*dimethylpyridino*(1′,2′-1,2)*imidazolium hydroxide*] (X; R = R′ = R‴ = Me, R″ = Ph), yellow prisms (from aqueous ethanol), exhibiting a green fluorescence in solution (43%, based on nitrile),

XUM

m. p. 170·5° (Found: C, 73·2; H, 6·3. $C_{18}H_{18}O_2N_2$ requires C, 73·5; H, 6·1%), $\lambda_{max.}$ 2650, 4000 Å in ethanol (ε 11,685, 7855).

N-Benzyl-N-2-quinolylglycine (XI).—*N-2-Quinolylaminoacetonitrile* was prepared as was the pyridyl-nitrile, crystallising from chloroform as brownish monoclinic prisms (49%), m. p. 188—191° (Found: C, 71·9; H, 5·05. $C_{11}H_9N_3$ requires C, 72·1; H, 4·9%). It (3 g.) was refluxed in benzyl chloride (10 ml.) for 48 hr., and the mixture poured into ether (100 ml.). The resultant brown solid was dissolved in ethanol (20 ml.), and the solution made just acid to Congo Red by the addition of concentrated sulphuric acid. In 24 hr. at −10°, *N-benzyl-N-2-quinolylaminoacetonitrile hydrogen sulphate* separated as prisms (3·7 g., 63·3%), m. p. 300° (decomp.) (from aqueous ethanol) (Found: C, 58·4; H, 4·5. $C_{18}H_{16}O_4N_3S$ requires C, 58·3; H, 4·3%).

This sulphate (3 g.) was refluxed for 4 hr. with 5N-hydrochloric acid (20 ml.). Considerable darkening occurred. When the brown oil which separated on cooling was washed with a large quantity of cold water it solidified. The solid crystallised from benzene–light petroleum (b. p. 40—60°), giving yellow needles (0·7 g.), m. p. 100° (after decomposing at 65°) (Found: C, 78·5; H, 5·5. $C_{18}H_{14}ON_2$ requires C, 78·7; H, 5·1%). $\lambda_{max.}$ 2210, 2780, 2850 Å in ethanol (ε 25,240, 12,162, 13,162). This substance corresponds to the unacetylated mesoionic *compound* (XII; R = H).

The residual acid hydrolysate was brought to pH 7 with saturated sodium hydrogen carbonate solution, a white solid separating. Crystallisation from ethanol gave the required *acid* (XI) (2·1 g., 54·6%) as prisms, m. p. 195—196° (Found: C, 73·9; H, 5·53. $C_{18}H_{16}O_2N_2$ requires C, 73·9; H, 5·5%).

Ring-closure. This acid was heated on the water-bath with acetic anhydride (10 ml.) for 2 hr. and worked up as previously. The benzene solution on concentration and cooling gave *anhydro-[4-acetyl-3-benzyl-5-hydroxyquinolino(1′,2′-1,2)imidazolium hydroxide]*, yellow prisms, m. p. 113—115° (0·7 g., 43%) (Found: C, 76·2; H, 5·3. $C_{20}H_{16}O_2N_2$ requires C, 76·0; H, 5·1%). Further concentration and cooling gave yellow needles (0·2 g., 12·3%) identical with the neutral product of the hydrolysate above.

N-Benzyl-*N*-2-quinolylglycine (1·0 g.) was refluxed for 24 hr. with 3N-hydrochloric acid (10 ml.). The dark solution was evaporated to dryness under reduced pressure and the solid residue extracted with benzene. Concentration and cooling yielded anhydro-[3-benzyl-5-hydroxyquinolino(1′,2′-1,2)imidazolium hydroxide] (XII; R = H) (0·13 g., 12%).

Attempts to Prepare N-2-Pyrimidylglycine.—Attempts to cyanomethylate the amino-group of 2-aminopyrimidine failed. Accordingly the reactions with chloroacetic acid and bromoacetic ester were examined.

(a) *Chloroacetic acid.* 2-Aminopyrimidine (2 g.) and chloroacetic acid (2 g.) were warmed on the water-bath for 0·5 hr. An intense purple colour developed. The mixture was evaporated to dryness under reduced pressure and the residue dissolved in ethanol (15 ml.). The solution was passed through a kieselguhr column (24″ × 1″), the purple pigment being strongly retained. Evaporation of the colourless ethanol passing through yielded 2-aminopyrimidine chloroacetate (3 g.), m. p. 91—93°. Elution of the column with 50% aqueous acetone and removal of the solvent gave hygroscopic crystals which could not be purified by recrystallisation. They were soluble in water and very soluble in sodium carbonate solution, developing a purple-red colour. The purple colour was regenerated by addition of acid. When 2-aminopyrimidine chloroacetate was heated to 240° for 1 hr., the purple compound was formed.

(b) *Bromoacetic ester.* 2-Aminopyrimidine (10 g.) and ethyl bromoacetate (5 ml.) were warmed together on the water-bath for 0·5 hr. The deep purple colour developed as previously and removal of the volatile components under reduced pressure and crystallisation from alcohol gave 2-aminopyrimidine hydrobromide (0·7 g.). The mother-liquor was passed through a kieselguhr column which retained the pigment. Elution with 50% aqueous ethanol and evaporation gave a solid which crystallised from methanol at −10° as black crystals with a golden sheen, m. p. >360°. This material was soluble in water and ethanol with a purple-blue colour and in sodium carbonate solution with a purple-red colour. Evaporation of the latter solution to dryness under reduced pressure provided a residue which was insoluble in ethanol. The original pigment (Found: C, 35·3; H, 4·4; N, 16·6%) was absorbed from aqueous solution by both base- and acid-ion exchange resins. The aqueous solution was bleached by concentrated nitric acid, the colour being regenerated on dilution. Addition of mercuric chloride to an aqueous solution precipitated an insoluble derivative. A similar pigment was obtained

XUM

from 2-methylaminopyrimidine. No corresponding colour was obtained when 2-amino-4-methylpyrimidine, guanine, or adenine was used as the amine.

N-Methyl-N-(N-phenylbenzimidoyl)aminoacetonitrile.—A mixture of benzanilide (20 g.) and thionyl chloride (30 ml.) was refluxed for 0·5 hr., the residual thionyl chloride being then evaporated under reduced pressure at 50° and the syrup remaining dissolved in light petroleum (b. p. 40—60°). The solution was freed from a small residual portion of benzanilide (0·3 g.) and evaporated to dryness on the steam-bath. The resulting oily *N*-phenylbenzimidoyl chloride solidified as a brown solid, m. p. 40° (19 g., 87%), and was sufficiently pure for the subsequent reaction.

N-Phenylbenzimidoyl chloride (10 g.) was dissolved in triethylamine twice redistilled from " Hi-drite " (20 ml.), the temperature being kept at 0°. Methylaminoacetonitrile (3·3 g.) was added slowly to the cooled mixture and stirring continued for 0·25 hr. The volatile components of the reaction were removed under reduced pressure at 60°, the solid residue was dissolved in hydrochloric acid, and the solution was filtered. The filtrate was made strongly alkaline with 3N-sodium hydroxide, and the separating oil extracted with ether which on evaporation yielded a solid. This was extracted with light petroleum (b. p. 60—80°) and on concentration yielded *N-methyl-N-(N-phenylbenzimidoyl)aminoacetonitrile* as monoclinic prisms, m. p. 106—107° (7 g., 65·5%) (Found: C, 77·0; H, 5·75; N, 16·8. $C_{16}H_{15}N_3$ requires C, 77·1; H, 6·0; N, 16·8%).

Ring-closure. The nitrile (5 g.) was refluxed with 2% hydrochloric acid (50 ml.) for 0·75 hr., then evaporated to dryness. Addition of excess of saturated aqueous sodium hydrogen carbonate dissolved all but a small amount of solid (which was filtered off). The filtrate, evaporated to dryness, gave a solid residue which gave a positive ninhydrin test. Acetic anhydride (25 ml.) was added, and the solution heated on the steam-bath for 1·5 hr., becoming dark brown immediately and developing a deep purple fluorescence. After cooling and filtration the acetic anhydride was evaporated under reduced pressure and final traces were removed by two evaporations with xylene. The residue was dissolved in benzene and decolorised with charcoal to give on concentration *anhydro-[4-acetyl-3-methyl-5-hydroxy-1,2-diphenylimidazolium hydroxide]* (XV; R = R′ = Ph, R″ = R‴ = Me), colourless plates, m. p. 243—244° (3 g., 55%) (Found: C, 74·2; H, 5·4. $C_{18}H_{16}O_2N_2$ requires C, 74·0; H, 5·5%), $\lambda_{max.}$ 2600, 3200, 3280 Å in ethanol (ε 8550, 16,150, 15,620).

A homologous *compound* was obtained in an identical manner by treating the amino-acid with propionic anhydride; this formed plates, m. p. 215°, from benzene (49%) (Found: C, 74·5; H, 5·9; N, 9·2. $C_{19}H_{18}O_2N_2$ requires C, 74·5; H, 5·9; N, 9·15%), $\lambda_{max.}$ 2660, 3200, 3280 Å in ethanol (ε 8220, 15,305, 14,805). Neither of these compounds was attacked by boiling benzylamine or warm dilute acid and alkali. They crystallised from a large quantity of water.

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE,
8, HUNTER STREET, LONDON, W.C.1.

[*Received, March 4th*, 1959.]

---

575. *Effects of γ-Radiation. Part IV.* The Degradation of* D-*Glucose in Aqueous Solution by γ-Irradiation* in Vacuo.

By P. M. GRANT and R. B. WARD.

The effect of ^{60}Co γ-radiation on aqueous solutions of glucose *in vacuo* has been studied. Gluconic acid and 2-oxo-D-*arabino*-aldohexose have been isolated as products; the latter has been determined by a new method utilising its ready reaction with *o*-phenylenediamine. Evidence for other products is presented and a degradation mechanism discussed.

INCREASING attention is being paid to the effect of radiation on solutions of sugars, and recently irradiation of oxygenated glucose solutions has been studied.[1] A number of other investigations have been made (see, *e.g.*, refs. 2, 3), but no definite degradation processes appear to have been proposed and substantiated for the evacuated system.

* Part III, *J.*, 1959, 2659.

[1] Phillips, Moody, and Mattock, *J.*, 1958, 3522.
[2] Wolfrom, Brinkley, McCabe, Shen-Han, and Michelakis, *Radiation Res.*, 1959, **10**, 37.
[3] Bothner-by and Balazs, *ibid.*, 1957, **6**, 302.

XUM

The present investigation arose from observations that the reducing power of irradiated maltose solutions decreased with increasing dose, although the formation of glucose could be readily detected by chromatography. This was not in agreement with findings, then incomplete, on the irradiation of glucose in oxygen,[4] which led one to expect the formation of uronic acids. Irradiation of evacuated maltose solutions was also shown to produce relatively large yields of acids and lactones, and some evidence for a structure of 2-oxo-D-*arabino*-aldohexose type was obtained (see below).

These studies indicated that the preliminary mechanisms advanced for oxygenated solutions were not valid for evacuated solutions. Consequently glucose solutions which had been irradiated with γ-rays *in vacuo* were freeze-dried and examined by paper chromatography and paper ionophoresis. Gluconic acid, 2-oxo-D-*arabino*-hexonic acid, arabinose, arabonic acid (trace), and glucosaccharic acid (trace) were among the products detected. Gluconic acid was present as the major product. When the irradiated solution was chromatographed and the " glucose " band cut out and eluted, the eluate, on chromatography in phenol–water, showed the presence also of 2-oxo-D-*arabino*-aldohexose. Glucuronic acid and 2-oxo-D-*arabino*-hexonic acid can only with difficulty be distinguished by chromatography. Additional evidence was obtained by oxidising the irradiated solution with alkaline hypoiodite before ionophoresis. Under these conditions uronic acids are oxidised to saccharic acids. This treatment did not increase the minute amount of saccharic present, indicating effective absence of glucuronic acid. This simple oxidation technique was later used to verify the presence of glucuronic acid in oxygenated systems.[1] It also shows that polyols are absent, in agreement with the complete absorption of the irradiated solute on excess of Amberlite IRA-400 resin (OH^- form).[5] 2-Oxo-D-*arabino*-aldohexose was identified by the preparation of glucose 2 : 4-dinitrophenylosazone at a low temperature under conditions which did not afford the derivative from glucose.

Gluconic acid was identified as its calcium salt, after partial purification on 2% cross-linked " micro-bead " Deacidite FF resin in the carbonate form.[6] The mixture of acids was eluted with N-ammonium carbonate. Although this mild resin-treatment caused some degradation of 2-oxo-D-*arabino*-hexonic acid and 2-oxo-D-*arabino*-aldohexose, it was shown that the degradation did not lead to gluconic acid. Further, the amounts of these labile compounds were relatively small, compared with that of gluconic acid.

Acid production (essentially gluconic acid in the early stages of the degradation) was measured over a range of doses by potentiometric titration. The large differences between the values obtained at pH 7 and pH 9 indicate lactone formation (Tables 1 and 2).

TABLE 1. *Radiation degradation of* 0·1% *glucose solution* in vacuo.

Total dose (10^{18} ev ml.$^{-1}$)	Gram-equiv. of carboxylic acid pH 7	pH 9·3	pH 10	2-Oxo-D-*arabino*-aldohexose yield (mg./g.)	log I_0/I (267 mμ)
0	~0	~0	~0	0	0·0013
1·14	0·003	0·005	0·006	3·2	0·0158
2·28	0·006	0·012	0·014	6·2	0·0548
4·56	0·013	0·026	0·033	12·8	0·0904
6·84	0·018	0·034	0·041	17·2	0·129
11·4	0·031	0·052	0·061	30·6	0·228
18·2	0·041	0·074	0·087	42·5	0·334

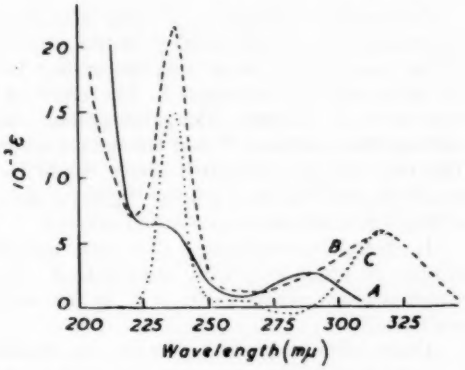
No satisfactory method was available for determination of 2-oxo-D-*arabino*-aldohexose.[7] It was found that *o*-phenylenediamine and 2-oxo-D-*arabino*-aldohexose gave 2-(*arabino*-tetrahydroxybutyl)quinoxaline quantitatively in oxygen-free water at 60°. This product differed markedly in ultraviolet absorption at 237 and 318 mμ from unchanged *o*-phenylenediamine and 2-oxo-D-*arabino*-aldohexose (see Figure). The 320 mμ region was chosen for

[4] Phillips, *Nature*, 1954, **173**, 1044.
[5] Barker, Bourne, Salt, and Stacey, *J.*, 1958, 2736.
[6] Machell, *J.*, 1957, 3389.
[7] Bayne and Fewster, *Adv. Carbohydrate Chem.*, 1956, **11**, 43.

TABLE 2. *Radiation degradation of* 0·1% *maltose solution* in vacuo.

Total dose (10^{18} ev ml.$^{-1}$)	Gram-equiv. of carboxylic acid pH 7	pH 8	pH 9	Reducing power (%)	log I_0/I (262 mμ)
0	0	0	0	100	—
19·7	0·053	0·054	0·09	89	0·32
53·5	0·15	0·19	0·23	81	0·70
74·0	—	—	—	79	0·85
150	0·34	0·40	0·45	67	1·22
380	0·50	0·59	0·66	59	1·61
760	0·55	0·69	0·77	44	2·17

the estimation of the 2-oxo-D-*arabino*-aldohexose, since it was free from interference caused by possible slight oxidation of the diamine. With *o*-phenylenediamine as control (Table 1) the amount of 2-oxo-D-*arabino*-aldohexose was calculated from the difference in molar extinction coefficient ($\Delta\varepsilon_{320} = 5600$). The absorption curve obtained under these conditions closely approximated to the theoretical difference curve (curve *C* in the Figure)



Spectrophotometric determination of 2-(arabino-*tetrahydroxybutyl)quinoxaline.*

A, o-*Phenylenediamine.*
B, 2-(arabino-*Tetrahydroxybutyl)quinoxaline.*
C, Differential molar extinction coefficient from B–A (Δε).

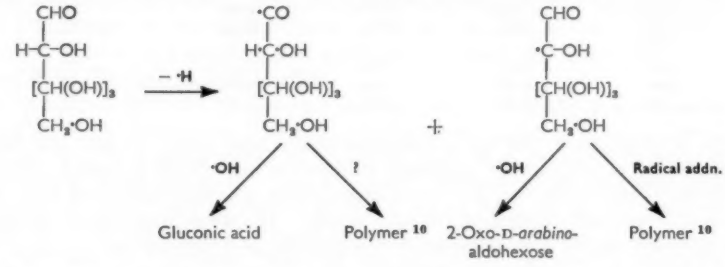
A similar curve was obtained when irradiated maltose solutions were heated with *o*-phenylenediamine in the same way, which indicates formation of maltosone.

Considerable interest has been shown in the ultraviolet absorption spectra of irradiated carbohydrate solutions.[1,3] The maxima occur at 262 mμ (maltose) and 267 mμ (glucose). 2-Oxo-D-*arabino*-aldohexose itself behaves similarly, but the absorption of the irradiated solution exceeded that calculated from the yield of this component. Glyceraldehyde in neutral or acidic solution shows negligible absorption, but 1 : 3-dihydroxypropan-2-one solutions slowly produce the observed absorption pattern, and this production has been advanced to explain the spectrum of glucose solutions irradiated in oxygen.[1] However, 1 : 3-dihydroxypropan-2-one has a molar extinction coefficient $\varepsilon_{270} \not> 30$ in neutral solution or at pH values between 3 and 7.[8] Hence to account for the spectrum this compound would have to be formed at a rate of 100 mg. l.$^{-1}$ hr.$^{-1}$ and would equal the initial weight of glucose within 10 hr. (Table 1). Even in 0·1N-sodium hydroxide the compound has $\lambda_{max.}$ ~290 mμ (ε 1000).[8] However, the required absorption maximum is given by enediol structures such as L-ascorbic acid ($\lambda_{max.}$ 263 mμ; ε 8500) in neutral or slightly acid solution. D-Glucoascorbic acid has been claimed as a product from the irradiation of gluconolactone in aqueous solution[9] and it has been found that irradiated glucose solutions readily decolorise dichlorophenolindophenol. However, these properties would be exhibited by any enediol structure which was not precluded by lactone-ring formation. Further, similar absorption is given by the polymeric materials produced from maltose, glucose, and gluconolactone on prolonged irradiation *in vacuo* (Part I[10]).

[8] Petuely and Meixner, *Monatsh.*, 1953, **84**, 1061.
[9] Coleby, *Chem. and Ind.*, 1957, 111.
[10] Barker, Grant, Stacey, and Ward, *J.*, 1959, 2648.

XUM

The degradation mechanism postulated is closely analogous to the radiation-induced degradation of glycollic acid (Parts II and III).[11] Primarily, a hydrogen atom is abstracted from the solute by solvent radicals, and the annexed sequence follows.



Irradiation of crystalline glycollic acid gives the carboxyhydroxymethyl radical,[12] and degradation of glycollic acid in dilute aqueous solution *in vacuo* is consistent with the initial formation of this radical, the product being modified by the presence of oxygen due to peroxy-radical formation.[11] The effect of radiation on crystalline glucose may be expected to be similar. The paramagnetic resonance spectra of a number of *X*-irradiated carbohydrates indicate [13] that the radical system is closely associated with a C_2 fragment. The two radicals postulated above would be in agreement with this. Further, autoradiolysis of C^{14}-labelled glucose [14] gives a mixture of degradation products similar to that obtained in dilute aqueous solution *in vacuo*.

It should be emphasised that early carbon–carbon scission is not precluded, but it appears to occur only to a small extent. Later in the degradation sequence carbon–carbon scission occurs easily, *e.g.*, in the oxidative decarboxylation of gluconic acid to arabinose.[2,15]

Degradation of glucose solutions by irradiation in the presence of oxygen might be expected to yield the same radicals, which would rapidly be converted into the corresponding peroxy-radicals, preventing radical addition but yielding essentially the same oxidised compounds. However, observations on the degradation of glucose solutions in oxygen [1] suggest that neither 2-oxo-D-*arabino*-aldohexose nor 2-oxo-D-*arabino*-hexonic acid is formed, but instead glucuronic acid is formed and extensive carbon–carbon scission occurs. This may be analogous to the carbon–carbon scission which occurs on irradiation of aqueous glycollic acid in oxygen and is reduced on irradiation of aqueous glycollic acid *in vacuo*.[11]

Experimental

Determination of 2-*Oxo*-D-arabino-*aldohexose*.—(i) *Preparation of* o-*phenylenediamine*, 2-*oxo*-D-arabino-*aldohexose and* 2-(arabino-*tetrahydroxybutyl*)*quinoxaline*. *o*-Phenylenediamine was recrystallised (charcoal) twice from oxygen-free hot water under nitrogen and dried *in vacuo*. The colourless material had m. p. 102°. The ultraviolet spectrum and molar extinction coefficients were $\lambda_{max.}$ 231 (ε 5400) and 288 mμ (ε 2750) (Figure).

2-Oxo-D-*arabino*-aldohexose [16] was purified by elution from a column of powdered cellulose with the organic phase of butan-1-ol–ethanol–water (4 : 1 : 5 v/v) and obtained as a pale yellow, amorphous, slightly hygroscopic solid. The material showed only one component on chromatography in the systems described below.

2-(*arabino*-Tetrahydroxybutyl)quinoxaline was prepared by warming 2-oxo-D-*arabino*-aldohexose (12 mg.) with *o*-phenylenediamine (11 mg.) in water (1 ml.) at 60° for 10 min. The

[11] Grant and Ward, *J.*, 1959, 2654, 2659.
[12] Grant, Ward, and Whiffen, *J.*, 1958, 4635.
[13] Williams, Geusic, Wolfrom, and McCabe, *Proc. Nat. Acad. Sci. U.S.A.*, 1958, **44**, 1128.
[14] Bourne, Hudson, and Weigel, unpublished work.
[15] Barker, Grant, Stacey, and Ward, *Nature*, 1959, **183**, 376.
[16] Fischer, *Ber.*, 1889, **22**, 87.

crystals deposited on cooling were filtered off, and after recrystallisation from water had m. p. 190°, $\lambda_{max.}$ 237·5 (ε 21,200) and 318 mμ (ε 5800) (Figure).

(ii) *Quantitative formation of* 2-(arabino-*tetrahydroxybutyl*)*quinoxaline from* 2-*oxo*-D-arabino-*aldohexose*. *o*-Phenylenediamine had unchanged ultraviolet absorption after being heated in oxygen-free water for 3 hr. under nitrogen at temperatures up to 100°.

2-Oxo-D-*arabino*-aldohexose (10·4 mg.) was heated in an oxygen-free solution of *o*-phenylenediamine (12 mg.) in water (6 ml.) at 60° under nitrogen and aliquot parts (1 ml.) were removed after 10, 30, 60, 90, and 120 min. Each aliquot part was diluted to 100 ml. and the absorption at 320 mμ determined against a control solution containing *o*-phenylenediamine (0·02 mg./ml.). By using the Δε curve of the Figure, $\Delta\varepsilon_{320} = 5600$ was obtained, enabling the apparent percentage conversion of 2-oxo-D-*arabino*-aldohexose into 2-(*arabino*-tetrahydroxybutyl)quinoxaline to be calculated. The values after the above periods of heating were 74, 90, 97, 96, and 97% respectively. It was concluded that the 2-oxo-D-*arabino*-aldohexose sample was 97% pure.

(iii) *Interference of glucose, gluconic acid and* 2-*oxo*-D-arabino*hexonic acid*. Glucose (1 g.), gluconic acid (45 mg.), and 2-oxo-D-*arabino*-hexonic acid (10 mg.) were separately heated in the absence of oxygen with 0·2% *o*-phenylenediamine solution (6 ml.) at 60° for 90 min. under nitrogen. The solutions were diluted a hundred-fold and the absorption at 320 mμ was measured against 0·002% *o*-phenylenediamine solution as described above. The three determinations gave absorption values of 0·006, −0·005, and −0·006 respectively, which were interpreted as effective errors of <2% in the determination of 2-oxo-D-*arabino*-aldohexose.

(iv) *Trial analysis of a weighed sample and a standard solution*. 2-Oxo-D-*arabino*-aldohexose (10·0 mg.) was heated with oxygen-free 0·2% *o*-phenylenediamine solution (6 ml.) for 90 min. at 60° under nitrogen. An aliquot part (1 ml.) was diluted to 100 ml., and the absorption at 320 mμ measured against 0·002% *o*-phenylenediamine solution. The absorption corresponded to 9·7 mg. of 2-oxo-D-*arabino*-aldohexose (97%).

A mixture containing glucose (0·507 g.), 2-oxo-D-*arabino*-aldohexose (8·0 mg.), 1 : 4-gluconolactone (18·3 mg.), and 2-oxo-D-*arabino*-hexonic acid (8·0 mg.) was estimated (as above) to contain 7·7 mg. (96·5%) of 2-oxo-D-*arabino*-aldohexose.

Irradiation of Solutions.—The sugar solution (0·1%) was degassed and irradiated in an evacuated sealed vessel by means of a 200 c ^{60}Co source at a dose-rate of $3{\cdot}8 \times 10^{16}$ ev min.$^{-1}$ ml.$^{-1}$, as described earlier.[10,11,15] The solution was freeze-dried.

Examination of the Irradiated Solutions.—Irradiated solutions (0·1%) of maltose and glucose were prepared. In general only the operations effected on the glucose solutions are described below. The results obtained from the less detailed treatment of the other solutions are discussed in the theoretical section.

(i) *Chromatographic and ionophoretic analysis*. Chromatography was in butan-1-ol–ethanol–water (4 : 1 : 5 v/v), butan-1-ol–propionic acid–water (6 : 3 : 4 v/v), butan-1-ol–water–90% formic acid (4 : 3 : 1 v/v), ethyl acetate–90% formic acid–acetic acid–water (18 : 1 : 3 : 4 v/v), and pentanol–water–90% formic acid (4 : 3 : 1 v/v). Ionophoresis was in 0·2M-acetate buffer (pH 5), 0·2M-borate buffer (pH 10), and 0·75M-formate buffer (pH 2). The components were developed with aniline hydrogen phthalate,[17] alkaline silver nitrate,[18] naphtharesorcinol,[19] and Chlorophenol Red.[20]

Glucose solution (0·1%), irradiated for 14 hr. (total dose $3{\cdot}2 \times 10^{19}$ ev ml.$^{-1}$), was examined by chromatography and ionophoresis. Comparison of a number of papers enabled some conclusions to be drawn in spite of rather extensive streaking. Gluconic acid, 2-oxo-D-*arabino*-hexonic acid, arabinose, arabonic acid (trace), and glucosaccharic acid (trace) appeared to be present among several other components. The first three appeared to be the major products. No glucuronic acid was found (see below). 2-Oxo-D-*arabino*-aldohexose was not separated from glucose by the solvents used. Consequently the "glucose" band was cut from a number of chromatograms on Whatman No. 3 paper which had been irrigated with the butan-1-ol–ethanol–water system. The bands were eluted and reapplied to a chromatogram which was eluted with phenol–water (3 : 1 w/w). On development, two spots were present, behaving identically with

[17] Partridge, *Nature*, 1949, **164**, 443.
[18] Trevelyan, Procter, and Harrison, *ibid.*, 1950, **166**, 444.
[19] Forsyth, *ibid.*, 1948, **161**, 239.
[20] Block, Durrum, and Zweig, "A Manual of Paper Chromatography and Paper Electrophoresis," Academic Press, New York, 1955, p. 169.

XUM

glucose and 2-oxo-D-*arabino*-aldohexose. On longer irradiation (>24 hr.) no interpretation could be put on the severely streaked chromatograms.

(ii) *Potentiometric titration.* The freeze-dried solids (0·2—1·6 g.) from solutions of glucose (0·1%) irradiated for various periods were dissolved in water (10 ml.) and titrated potentiometrically, under nitrogen, with carbonate-free 0·0217N-sodium hydroxide. Between pH 7·5 and pH 9·2, the immediate pH change on addition of alkali was followed by a slow drift towards neutrality. This is similar to the behaviour of a typical lactone such as 1 : 4-gluconolactone.

Control titrations on equal weights of glucose were made and subtracted from those for the irradiated materials. The results (Tables 1 and 2) are expressed in terms of acidimetric equivalent weights per mole of original sugar at various pH values.

(iii) *Ultraviolet absorption spectra.* The freeze-dried solid from irradiated solutions was dissolved in water (5 ml.) and its ultraviolet absorption spectrum measured. In all cases a maximum occurred in the range 260—270 mμ (Tables 1 and 2).

(iv) *Infrared absorption spectra.* These were measured for the freeze-dried solutes.

(v) *Reducing power.* Irradiated maltose solution (2 ml.), after various doses, was treated by Shaffer and Hartmann's method [21] to determine the reducing power. The determinations were unaltered by prior adjustment of the irradiated solution to pH 7 with alkali and addition of catalase to destroy any hydrogen peroxide (Table 2).

(vi) *Glucuronic acid.* Irradiated glucose solutions (100 ml.) were freeze-dried and treated with iodine solution [4 ml., containing iodine (8·47 g./l.) and potassium iodide (16·7 g./l.)] and N-sodium hydroxide (0·4 ml.). The solution was left at room temperature for 15 min., then neutralised with excess of solid carbon dioxide. The solution was then subjected to paper ionophoresis in 0·2M-acetate buffer (pH 5) and developed with alkaline silver nitrate.[18] Glucosaccharic acid was not formed, and no immobile components (*e.g.*, polyols) remained; components were detectable only in the hexonic acid region.

(vii) *Polyols.*[5] Amberlite IRA-400 resin (5 ml.) was washed with N-sodium hydroxide saturated with barium hydroxide (25 ml.) and then with carbon dioxide-free water (250 ml.). The freeze-dried solute from irradiated glucose (27 mg.) was dissolved in water (10 ml.) and applied to the column which was eluted with water (50 ml.). The eluate was freeze-dried to yield a trace of residue which showed no trace of polyols on chromatography and development with alkaline silver nitrate.

Characterisation of Products.—(i) 2-*Oxo*-D-arabino-*aldohexose.* The freeze-dried solute from irradiated glucose solution (1 g.) was dissolved in water (250 ml.), and the solution filtered and cooled to 15°. A filtered solution of 2 : 4-dinitrophenylhydrazine [250 ml., containing 5 g. in 2N-hydrochloric acid (300 ml.)] was warmed to 50° and added with rapid stirring. The solution was kept at 35° and filtered after 15 min. The product (58 mg.), recrystallised twice from aqueous ethanol, had m. p. 251° unaltered on admixture with authentic glucose 2 : 4-dinitrophenylosazone. 2-Oxo-D-*arabino*-aldohexose yielded an identical product on similar treatment, but glucose gave no precipitate at 35° in 2 hr., although it rapidly gave the same product at 100°.

(ii) *Gluconic acid.* The freeze-dried solute from irradiated solution of glucose (2 g.) was stirred for 2 hr. with Deacidite FF microbead resin (200—400 mesh; 2% nominal cross-linking; the carbonate form) (40 ml.).[6] The resin was then packed into a column and eluted with water (250 ml.) and N-ammonium carbonate (250 ml.). The ammonium carbonate eluate was treated with excess of Zeo-Karb 225 (H^+ form) and passed immediately into a stirred suspension of calcium carbonate. The mixture was stirred for 72 hr., boiled, and filtered (charcoal). The solution was concentrated, and the crude calcium salt precipitated by ethanol was recrystallised from water at 0° (yield 0·121 g.).[22] The product had $[\alpha]_D^{20}$ 8·5° (*c* 1·9 in water) and showed only one component corresponding to gluconic acid on chromatography and ionophoresis.

The authors thank the United Kingdom Atomic Energy Authority, Research Group, Harwell, for supporting these investigations and for maintenance grants, and Professor M. Stacey, F.R.S., and Dr. S. A. Barker for their interest.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, March 10th,* 1959.]

[21] Shaffer and Hartmann, *J. Biol. Chem.*, 1921, **45**, 349, 365.
[22] Hudson and Isbell, *J. Amer. Chem. Soc.*, 1929, **51**, 2225.

576. *Submicro-methods for the Analysis of Organic Compounds. Part VIII.* Factors associated with Submicro-titration in Glacial Acetic Acid.*

By R. Belcher, J. Berger, and T. S. West.

Factors associated with the submicro-titration of organic compounds as bases in glacial acetic acid, and the evolution of a technique of potentiometric and visual submicro-titration in such a medium, are studied. Those which require careful control are the method of use of burettes with organic solvents, the weighing and dissolving the sample, the choice of the correct visual indicator shade to mark the equivalence-point, the use of colour comparison solutions, the method of determining the blank (control) analysis, and the water content of the solvent.

Many organic compounds can be titrated as acids or bases, but water is not generally a suitable medium. Consequently they are frequently determined by titration in non-aqueous solvents, *e.g.*, glacial acetic acid for bases, and basic solvents such as butylamine for acids. Many such determinations have been described on the macro-, semimicro-, and micro-scales. Since the submicro-titrations hitherto described in this Series have been carried out in aqueous media and the technique of non-aqueous titrimetry differs substantially, it was necessary to examine various factors associated with the use of organic solvents on this scale before developing analytical methods. These investigations are now described, and the analytical methods will be described later.

Titration of Organic Bases in Glacial Acetic Acid.—The use of glacial acetic acid as solvent for the titration of organic bases is well established on the conventional scales of working.[1] Perchloric acid in acetic acid is most frequently used as titrant since it is the strongest acid in this medium and is very stable. The reagent is readily prepared from *ca.* 70% aqueous perchloric acid by dilution with acetic acid. The water content can be measured by titration with Karl Fischer reagent and its concentration suitably adjusted by addition of acetic anhydride.

Primary Standards.—Potassium hydrogen phthalate was selected as primary standard. Although objections have been raised to its use in macro-titrations because of its low solubility it was found that 50 μg. samples dissolved readily (with stirring) in the amounts of solvent required and no visible precipitate of potassium perchlorate was produced immediately. In macro-titrations, high equivalent weight is desirable in a primary standard, but on the submicro-scale, where weighings can be done comparatively more accurately than titration (*i.e.*, with commercial syringe pipettes), the position is reversed.

Titration Equipment.—A suitable volume for the titration is 400 μl. (0·4 ml.) and a convenient shape of vessel approximates to a small test-tube, 11 mm. in internal diameter and 30 mm. long. When it is necessary to stopper such vessels, ordinary cork protected by thin Polythene sheet should be used, since the water in cork or in rubber is extracted by anhydrous acetic acid and interferes. The burettes used were identical with those used previously, but phenomena scarcely noticed with aqueous solutions became of prime importance with acetic acid solutions. Thus, after a syringe had been filled, the liquid was observed to rise quickly in the delivery tip of the capillary. It was found that the solvent evaporated round the plunger and not from the tip of the burette. Thus one burette lost 4·4 μl. in 90 min. Accordingly this effect must be guarded against and the time required for two titrations should not differ by more than 3—5 min.

Volatile Samples.—Samples were weighed as described previously, but although some compounds can be stored for days after weighing without appreciable loss, *e.g.*, potassium

* Part VII, *J.*, 1959, 2585.

[1] Round Table Discussion of Amer. Chem. Soc., *Analyt. Chem.*, 1952, **24**, 310.

XUM

hydrogen phthalate, others lose weight steadily, *e.g.*, *p*-bromoaniline, 1-naphthylamine, benzoic acid, and *p*-anisidine (see Table 1), and some, *e.g.*, *p*-toluidine, are so volatile that they cannot be weighed on the sensitive submicro-balance. It is therefore necessary to dissolve samples immediately after weighing.

TABLE 1. *Volatilisation of* p-*anisidine during storage in a platinum boat inside a micro-desiccator, removed only for weighing.*

Storage period (hr.)	0	1	2	3	19	43
Wt. of sample (μg.)	72·6	70·2	68·3	66·1	50·9	30·9
Loss (%)	—	3·3	5·9	9·0	29·9	57·4

Visual Indicators.—The choice of indicator is extremely important. We examined most of those recommended for use on the macro-scale, *viz.*, Crystal Violet, Methyl Violet, Ciba Blue BZL, Oracet Blue B, and Neutral Red. We cannot recommend the last three for submicro-titration because of the indistinct nature of the colour change and the high indicator correction. Crystal Violet and Methyl Violet are equally good, but the former is preferred since it can be used in lower concentration and, as will be seen later, this is important. Ellerington and Nicholls [2] described the colour change of Crystal Violet at the end-point as follows: [Base in excess] Violet → blue-violet → blue → green-blue → blue-green → green → yellow-green → green-yellow → yellow [acid in excess]. In submicro-titration the whole colour change from violet to green requires only 0·2—0·4 μl. of 0·01N-perchloric acid. Adjustment to a *fixed* colour can be done very accurately, particularly when a comparison solution is used.

Colour-comparison solutions. The colour-comparison solutions recommended by Ellerington and Nicholls are insufficiently stable for use in submicro-titration, but Gremillion's observation [3] that the titration curve of urea in acetic acid is virtually straight provided the necessary means of devising one. The colour of comparison solutions thus made is independent (visually) of the water content from 0·02 to 0·2% of water.

The selection of the correct shade for the indicator at the end-point, *i.e.*, the correct pH at which to stop titration, is of the utmost importance. In theory, it is necessary to establish the correct shade for each individual base, but we found by submicro-potentiometric titrations of very many bases that the colour of Crystal Violet at equivalence is near to royal blue. Accordingly a colour-comparison solution of this colour was prepared by addition of 0·1N-perchloric acid to urea in glacial acetic acid. This colour is not the *exact* colour observed with *all* bases, but it is sufficiently near to eliminate serious error. Even for an individual base, the blue colour at the equivalence point is slightly different for 40 μg. and 60 μg. samples. For a base which is weak in glacial acetic acid, *e.g.*, lithium benzoate, the colour change in a submicro-titration is near to blue-green and the change is spread over a fairly wide range.

Volume of Medium and Determination of "Blank."—The consumption of 0·01N-perchloric acid in a submicro-titration is 30—50 μl. If a large amount of solvent (1—2 ml.) is used, the blank analysis will be *ca.* 10% of the total titre, the visual end-point will be poor and the potential change in the potentiometric titration small. The smallest possible volume which we could use in the potentiometric titration was 0·4 ml., at which (see Table 2) the potentiometric blank is 1 μl. According to Kolthoff and Bruckenstein [4] the equivalence potential (or pH) in the titration of a base in glacial acetic acid is independent of the concentration of the base or salt so that the blank titration is established by titrating to the appropriate pH. The "blank" value increases with the amount of solvent. The values are reproducible ±0·1 μl.

Conant and Werner [5] noted that ionic strength considerably affects the colour behaviour

[2] Ellerington and Nicholls, *Analyst*, 1957, **82**, 233.
[3] Gremillion, *Analyt. Chem.*, 1955, **27**, 133.
[4] Kolthoff and Bruckenstein, *J. Amer. Chem. Soc.*, 1957, **79**, 1.
[5] Conant and Werner, *ibid.*, 1930, **52**, 4436.

of indicators in glacial acetic acid. We observed that whereas 50 μg. of sodium acetate titrated with 0·01N-perchloric acid give a blue colour with Crystal Violet at the end-point, 300 μg. titrated in the same way to the same pH (and with the same equivalence) give a blue-green end-point. The potentiometric blank remained unchanged but the visual

TABLE 2. *Dependence on the amount of solvent of visual and potentiometric blanks.*

Acetic acid (*ca.* 0·02% H_2O) (ml.)	0·2	0·4	0·6	0·8	1·0	1·2
Potentiometric blank (μl.)	—	1·0	1·5	2·0	2·4	2·6
Visual blank (blue) (μl.)	0·9	1·2	1·8	2·4	3·2	3·4

blank had increased. Kolthoff and Bruckenstein derived a quantitative expression and found that the ratio between the concentrations of the acid form and basic form of the indicator is proportional to the square-root of the concentration of the salt.

This effect which is not found in aqueous titrimetry means that even if a visual blank is determined for the solvent, it will not be reliable. Table 2 shows that the difference between potentiometric and visual blanks increases with increasing amounts of solvent. Such problems do not arise in the macro-scale since no significant blank is found.

FIG. 1.

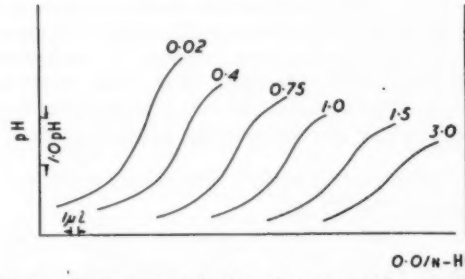
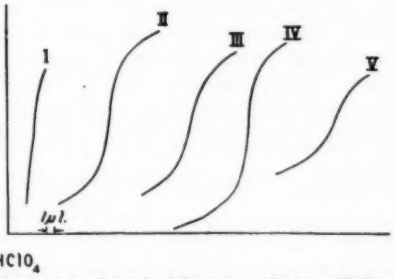


FIG. 2.



0·01N-$HClO_4$

FIG. 1. *Potentiometric titration of* ca. 50 μg. *of* p-*anisidine in* 0·4 *ml. of glacial acetic acid of specified water content* (%). *Silver–silver chloride/glass electrode system. Salt bridge electrolyte* 0·02N-*sodium perchlorate in acetic acid.*

FIG. 2. *Experimental procedure as in Fig.* 1, *but with water content controlled at* ca. 0·1%. I, Blank on 0·4 ml. glacial acetic acid. II, Titration of *ca.* 50 μg. of potassium hydrogen phthalate. III, Titration of *ca.* 50 μg. of sodium acetate trihydrate. IV, Theoretical curve for sodium acetate (no volume change). V, as III but without salt bridge.

Permissible Water-content of Solvent.—In macro-titrations, acetic acid containing up to 1% of water can be used safely as a solvent for the titration of most bases. According to Kolthoff and Bruckenstein the basic dissociation constant of water in glacial acetic acid is $pK = 12·53$ (cf. sodium acetate, $pK = 6·68$). The effect of water therefore becomes most pronounced near the end-point when it competes with the indicator (a weak base) for the perchloric acid. On the submicro-scale, we have found that water only slightly

TABLE 3.—*Dependence on the water content of glacial acetic acid of visual and potentiometric blanks.*

Water content of 0·4 ml. of acetic acid (%)	*ca.* 0·02	0·2	0·5	0·75	1·0	1·5	2·0
Potent. blank (μl.)	1·0	1·0	1·1	1·1	1·2	1·2	—
Visual blank (blue colour) (μl.)...	1·2	1·4	1·9	2·3	3—3·5	4—5	6—7
Remarks on the visual end-point	Good	Fairly good	Indefinite	Indefinite	Bad	Bad	Very bad

increases the potentiometric blank but adversely affects the slope of the curve and the magnitude of the potential break (cf. Table 3 and Fig. 1). The practical upper limit for water content is *ca.* 1·5%.

On the other hand, the visual blank increases considerably with concentration of

XUM

water and the colour change is drawn out. It was finally concluded that the water content should not greatly exceed 0·15—0·2% in submicro-work.*

The coefficient of cubic expansion of glacial acetic acid is *ca.* four times that of water. It is therefore desirable to apply a normality correction if the temperature varies by more than 2° from that at which the solution was standardised. This correction is 0·1% per °C.[6]

Comparison between Experimental and Theoretical Data.—According to the calculations and experimental data of Kolthoff and Bruckenstein,[4] the pH of 0·01N-perchloric acid in glacial acetic acid is 3·44 and of 0·01N-sodium acetate 10·11, *i.e.*, a pH interval of 6·67. In our experiments the difference was found to be 6·2. Fig. 2 shows, *inter alia*, the calculated and experimental curves for the titration of 0·001N-sodium acetate with 0·01N-perchloric acid. The experimental curve was obtained by use of a glass indicator against a silver–silver chloride reference electrode. The stability of the glass electrode increased considerably if it was stored permanently in glacial acetic acid solution. The difference between the experimental and the theoretical data is attributed to the uncertainties introduced by using glacial acetic acid with a higher water content than used by Kolthoff and Bruckenstein (<0·01%) and the use of a glass electrode which has been stored in glacial acetic acid for some months.

Table 4 reveals that the standard deviation on a series of standardisations of perchloric acid with potassium hydrogen phthalate is *ca.* ±0·5%, whilst for visual titration it is ±0·7%. The normalities determined by these methods differ by 1%. This divergence is attributed to the difference in blank value and to the time required to complete a titration (2 min. visually, 8 min. potentiometrically). The effect of the time factor on such titrations has already been mentioned. From these data we conclude that it is necessary to establish two normalities, one for visual and the other for potentiometric use.

TABLE 4. *Standardisation (normality* ×100) *of* 0·01N-*perchloric acid against potassium hydrogen phthalate* (50—70 μg.)

Potent.	1·041	1·037	1·036	1·037	1·028	1·034	1·031	1·040
Visual	1·041	1·057	1·045	1·059	1·041	1·053	1·058	1·041
Potent.	1·036	1·040	1·040	1·047.		Average 1·037; s.d. ± 0·0050		
Visual	1·045	1·050	1·042	— .		Average 1·048; s.d. ± 0·0073		

Stability of Solutions.—Data for the stability of perchloric acid in acetic acid are not available in the literature, though several workers have commented favourably on the reagent. Ellerington and Nicholls [2] reported that 0·1N-reagent requires standardisation every 3 days (but more recently they obtained solutions of satisfactory stability [7]). In view of this, the present study included stability tests on 0·1N- and 0·01N-reagents stored in 1 l. volumetric flasks with the glass stoppers covered with Polythene sheet. Several times each week small samples were analysed. The 0·1N-solution gave an unchanged titre during nine months, and the 0·01N-solution can be used for at least 1—2 months without standardising.

The stability of 0·01N-sodium acetate in acetic acid was also satisfactory. A change of only 0·3% occurred during 35 days. The colour comparison solutions faded gradually on standing in daylight for several weeks, but a solution stored in darkness for 2 months showed no visual difference in shade from a fresh one.

EXPERIMENTAL

Reagents.—(1) Acetic acid with water content adjusted to 0·02—0·15%. This is the "glacial acetic acid" used. (2) Potassium hydrogen phthalate, "Analar," finely powdered.

* Because of the influence of water all apparatus must be rinsed out thoroughly with glacial acetic acid containing Crystal Violet indicator and sufficient perchloric acid just to yield the green colour. The washings must be continued till the green colour of the solvent persists. A last washing must be done with pure glacial acetic acid.

[6] Seaman and Allen, *Analyt. Chem.*, 1951, **23**, 592.
[7] Ellerington and Nicholls, personal communication.

(3) Crystal Violet indicator solutions, 0·01% w/v and 0·5% w/v in glacial acetic acid. (4) 0·1N-Perchloric acid in acetic acid: 8·50 ml. of "AnalaR" 72% perchloric acid are added to 500 ml. of glacial acetic acid and 20 ml. of "AnalaR" acetic anhydride with agitation below 60—70°. The solution is diluted to 1 l. with glacial acetic acid and after standing for 24 hr. the water content is adjusted to 0·02—0·15%. (5) 0·01N-Perchloric acid in acetic acid, prepared by dilution of (4). (6) Blue comparison solution: 0·6 g. of urea in 70—80 ml. of glacial acetic acid treated with 3·3 ml. of 0·01% Crystal Violet indicator and 3·0 ml. of 0·1N-perchloric acid in acetic acid and diluted to 100 ml. (7) Blue-green comparison solution; prepared as above except that 6·0 ml. of 0·1N-perchloric acid in acetic acid are added. (8) Salt bridge electrolyte: 0·02N-sodium perchlorate monohydrate in glacial acetic acid.

Apparatus.—(1) Submicro-balance.[8] (2) Titration vessels: these must be washed as described already, dried by a stream of dry nitrogen, and stoppered with a cork covered with Polythene sheet. (3) "Agla" glass syringes: these must be used as described above. Minimum evaporation from the plunger is usually established in 15 min. (4) Magnetic stirrer used with glass-encased rotors 3 mm. long, external diameter *ca.* 1 mm. (5) "Daylight" blue bulbs (230 v, 60 w Mazda, BTH single coil) clamped, *ca.* 15 cm. above titration platform. The illumination is used only near the end-point to minimise errors due to heating of the syringe. (6) pH Meter: "Vibron Electrometer" Model 33-B and "Vibron pH Measuring Unit," Model C-33-B, Electronic Instruments Ltd., Richmond, Surrey, was used to give a pH discrimination of 0·002 pH unit. A Weston cell and circular potentiometer (1 megohm) was placed in series with the electrodes to obtain correct polarity and to adjust scale readings. The instrument was used on "negative input," and with full-scale deflection equal to one pH unit. (7) Glass electrode. Diameter of bulb 3·5 mm., diameter of stem, 3·5 mm., stem bent at right-angles *ca.* 4 cm. above bulb. This electrode was made to our specifications by Electronic Instruments Ltd. Design No. SK 605. (8) Silver–silver chloride electrode. Platinum disc 2—3 mm. in diameter sealed into 4 mm. glass tube, disc silvered and coated with AgCl by anodic treatment (total length of electrode 14 cm.). (9) Salt bridge: 7 mm. glass tubing drawn out to end in 1 cm. long capillary of 3 mm. external diameter, total length of bridge 5—6 cm. The capillary was stopped up with asbestos so that the leak rate from the assembled electrode and bridge was *ca.* 1 ml. in 4—5 days. The silver–silver chloride electrode was sealed into this salt bridge with a small rubber stopper.

Procedure.—The sample was weighed on the submicro-balance and transferred to the titration vessel in the usual way (see previous Parts).

(a) *Potentiometric method.* 0·4 ml. of glacial acetic acid was added from a 2 ml. graduated pipette, followed by one drop of 0·01% Crystal Violet and a rotor. The vessel was stoppered with a Polythene-protected cork and the contents were stirred magnetically for 3 min. The presence of the indicator warns of the approach of the end-point. The electrodes which had been stored in glacial acetic acid were wiped with filter paper and placed in a titration vessel containing 0·4 ml. of glacial acetic acid and a drop of 0·01% Crystal Violet and a rotor. The pH on the pH meter is then adjusted to *ca.* 8·5 by means of the potentiometer; this empirical value allows readings to be taken over the entire range of a submicro-titration. There may be a small drift after the adjustment as pH in pure acetic acid is not very well defined. With the titration equipment thus prepared, the glass electrode was first placed in the vessel containing the dissolved sample, then the burette tip (duly wiped with filter paper wetted with glacial acetic acid) and finally the salt bridge of the silver–silver chloride electrode.

In the vicinity of the end-point, the titrant was added in 1 μl. increments and the pH meter was read 15—20 sec. after each addition. The time required for titration carried out at a suitable rate was 7—8 min. The end-point was calculated according to the conventional second-derivative method.

Blank determinations were carried out as above with omission of the sample. The titration was begun in this instance by adding 0·4 μl. of 0·01N-perchloric acid twice and making further additions in 0·2 μl. lots. The readings were taken 30 sec. after each addition. The titration was continued well beyond the equivalence pH found in the actual determination. The blank analysis corresponded to the amount of perchloric acid required to obtain the equivalence pH. A typical value was 1·0 ± 0·1 μl. of 0·01N-perchloric acid. In each case the average of three determinations was chosen.

(b) *Visual indicator method.* The sample was weighed and dissolved as above and the

[8] Asbury, Belcher, and West, *Mikrochim. Acta*, 1956, 598.

titration was carried out till the same blue colour was obtained as that of the comparison solution which was placed in a similar vessel alongside the titration tube. The end-point was usually detected within ±0·1 μl. especially when a small over-titration was used. The time required for a visual titration was 2 min.

The blank, which was usually reproducible within ±0·1 μl., was determined by titrating the solvent to the same blue colour as above. Again the average of three blank determinations was taken.

One of us (J. B.) thanks the Carlsberg–Wellcome Foundation for a travelling fellowship.

CHEMISTRY DEPARTMENT, THE UNIVERSITY, BIRMINGHAM, 15. [*Received, March 13th,* 1959.]

---

577. *Submicro-methods for the Analysis of Organic Compounds. Part IX.*[1] *Titration of Organic Bases and Amine Hydrohalides in Glacial Acetic Acid.*

By R. BELCHER, J. BERGER, and T. S. WEST.

Procedures are described for the submicro-determination of organic bases, amine hydrohalides, quaternary ammonium salts, and primary aromatic amines and their hydrohalides by titration with 0·01N-perchloric acid in acetic acid in glacial acetic acid. Potentiometric and visual indicator methods (with Crystal Violet) are described. Hitherto undetected inaccuracies in macro-methods have shown on the submicro-scale and have been accounted for. The results obtained for primary aromatic amines and their hydrohalides are invariably high because of acetylation. An accuracy of *ca.* ±1% is usual.

VARIOUS factors which influence the titration of organic compounds as bases in glacial acetic acid on the submicro-scale of working have already been discussed.[1] We now apply such procedures to analysis.

(a) *Titration of Bases.*—Many organic compounds behave as bases in glacial acetic acid, *e.g.*, salts of carboxylic acids. Other substances can readily be converted into derivatives which behave as bases, *e.g.*, alcohols can be converted into xanthates and titrated with perchloric acid.[2] Carboxylic acids which are difficult to isolate pure can be determined similarly, *via* their *S*-benzylthiuronium salts,[3] whilst alcohols and alkyl halides can be dealt with as their *S*-alkylthiuronium picrates.[4] Table 1 summarises the results for several types of compound, and compares potentiometric and visual-indicator values on the submicro-scale with those obtained by macro-analysis. Submicro-procedures are satisfactory and a precision of ±1% is easily obtainable. Most compounds in Table 1 are easily dissolved in glacial acetic acid, but difficulty was encountered with the amino-acids. Since their perchlorates are much more soluble [5] they were dissolved in a slight excess of perchloric acid in acetic acid and the excess was determined by titration with sodium acetate. A similar back titration was used to analyse potassium ethyl xanthate since its decomposition, giving titratable potassium acetate, was too slow in acetic acid alone.

$$EtO{\cdot}CS_2K + Me{\cdot}CO_2H \longrightarrow EtO{\cdot}CS_2H + Me{\cdot}CO_2K$$

In most cases, a 50—60 μg. sample was used, but to ensure a reasonable titre, larger samples were taken of narcotine whose equivalent weight is much higher than that of the other substances examined.

[1] Part VIII, Belcher, Berger, and West, preceding paper.
[2] Berger, *Acta Chem. Scand.*, 1952, **6**, 1564.
[3] *Idem, ibid.*, 1954, **8**, 427.
[4] Schotte and Veibel, *ibid.*, 1953, **7**, 1357.
[5] Nadeau and Branchen, *J. Amer. Chem. Soc.*, 1935, **57**, 1363.

XUM

A blue comparison solution [1] was used for all the visual end-points except for that with lithium benzoate where the blue-green solution was used. In the potentiometric titration of lithium benzoate, the first derivative was considerably smaller than in the titration of the other compounds. The macro-titrations were preferred with visual indication of the end-point.

(b) *Titration of Amine Hydrohalides and Quaternary Ammonium Compounds.*—Whereas the salts of organic bases with oxalic acid, picric acid, etc., can readily be titrated as bases

TABLE 1.

Compound (M.W.)	Range of sample wts. (μg.)	No. of detns.	Equivalent wt. (average) Visual indicator	Potentiometric	Macro	Range of errors (%) Visual	Potentiometric
Sodium acetate trihydrate (136·1) ...	47·64—82·49	10	137·1	135·0	136·3	0·3—1·6	0·0—2·0
Sodium benzoate (144·1)	48·62—71·06	6	144·3	144·3	144·8	0·3—0·8	0·3—1·2
Lithium benzoate (128·05)	46·94—63·10	6	131·0	130·3	129·3	1·2—3·4	1·6—2·8
Ammonium succinate (152·15)	41·51—94·30	6	77·4	78·0	76·8	0·5—2·3	1·7—2·4
Potassium ethyl xanthate (160·29) *	43·66—69·65	6	158·0	158·3	160·6	1·0—3·3	1·6—2·8
S-Benzylthiuronium valerate (268·4) ...	55·54—82·49	6	267·5	271·2	268·7	0·4—3·2	1·3—3·5
S-Ethylthiuronium picrate (333·29) ...	92·85—142·3	6	335·6	334·0	333·4	2·1—2·6	0·2—2·3
Narcotine (413·41) ...	109·2—200·0	8	412·8	413·4	413·7	0·1—1·0	1·5—4·4
Atropine (289·36) ...	91·0—120·9	6	287·3	292·1	289·8	0·1—5·5	1·6—4·1
DL-α-Alanine (89·09)	47·24—72·90	10	87·9	87·8	88·9	0·2—2·3	0·5—1·8
Glycine (75·07)	45·8—7[illegible]·38	8	73·9	73·8	75·3	0·7—1·5	0·0—2·7

* Back titration.

in acetic acid, those of the halogen acids are not amenable to similar treatment. For such salts two methods have been devised: (1) The solution is boiled during titration to expel the halogen acid,[6] and (2) the compound reacts with excess of mercuric acetate:[7]

$$Hg(O_2CMe)_2 + 2BH^+Cl^- \rightleftharpoons HgCl_2 + 2BH^+,MeCO_2^-$$

In the second method, the excess of mercuric acetate is undissociated and is not titrated by perchloric acid, whereas the acetate of the base behaves as a strong base. The first procedure is less satisfactory both with respect to difficulties in the manipulation of boiling glacial acetic acid and to the possibility of decomposition of the organic compound.

TABLE 2.

Compound (M.W.)	Range of sample wts. (μg.)	No. of detns.	Equivalent wt. (average) Visual indicator	Potentiometric	Macro	Range of errors (%) Visual	Potentiometric
Cocaine hydrochloride (339·8)	72·63—127·7	9	339·6	341·6	342·8	0·1—3·5	0·6—3·4
Ephedrine hydrochloride (201·7)	57·37—75·13	6	200·0	203·6	202·2	1·2—2·5	0·7—3·4
Tetramethylammonium iodide (201·1)...	49·32—67·01	6	199·2	198·4	201·2	1·6—2·4	1·0—3·2
Di-n-butylamine hydrochloride (165·7)	46·77—61·36	6	164·4	164·4	166·1	0·8—2·0	0·4—2·5
Triethylamine hydrobromide (182·1) ...	48·40—74·83	6	181·7	183·7	182·7	0·2—2·7	0·6—2·2

On the submicro-scale we examined only the mercuric acetate method. To ensure that the reagent solution was standardised under the conditions of the determinations

[6] Higuchi and Concha, *J. Amer. Pharmaceut. Assoc., Sci. Edn.*, 1951, **40**, 173; *Science*, 1951, **113**, 210.

[7] Pifer and Wollish, *Analyt. Chem.*, 1952, **24**, 300.

XUM

S-benzylthiuronium chloride (by the mercuric acetate method) was used as primary standard.[3] The normality found by this procedure differed insignificantly from that obtained against potassium hydrogen phthalate. Although previous authors [7,8] have stressed the importance of not exceeding a one-fold excess of mercuric acetate we were unable to find any necessity for this on the submicro-scale. The results obtained on 60 μg. amounts of *S*-benzylthiuronium chloride were the same with two-, six-, and even twelve-fold excesses of mercuric acetate. Accordingly an amount corresponding (on average) to a six-fold excess was used for further submicro-titrations. The purity of the mercuric acetate is important.

The blank (control) analysis increased although the same solvent was used as in the foregoing titrations and was independent of the amount of mercuric acetate. The increase in titre was found to be due to reaction of the Crystal Violet (hexamethylpararosaniline chloride) with the mercuric acetate.

The data for visual and potentiometric analyses of five compounds are given in Table 2. The accuracy and precision are of the same order as before. Three minutes' stirring time was sufficient to dissolve most of the compounds except tetramethylammonium iodide which required *ca.* 15 min. Samples larger than 50—60 μg. were used for cocaine hydrochloride because of its high equivalent weight.

In the visual titration the blue matching solution was used to help in detection of the end-point.

(c) *Determination of Primary Aromatic Amines and their Hydrohalides.*—Keen and Fritz [10] described a micro-method for the titration of 0·2—4 mg. of aromatic amines. They were able to titrate *ca.* 400 μg. of aniline dissolved in 1 ml. of acetic acid with an error of *ca.* 0·5%. We have repeated their experiment potentiometrically with 1-naphthylamine [1] and the apparatus previously described. Table 3 shows that the result is dependent on the water content of the solvent. It is apparent that acetylation occurs to the extent of 10% if the water content of the solvent is *ca.* 0·02% (Karl Fischer determination). With a water content of 0·15% as much as 5% of acetylation takes place, but with a solvent containing 0·6—1·0% of water only slight acetylation occurs.

TABLE 3. *Equivalent weights found by potentiometric titration of* ca. 400 μg. *of* 1-*naphthylamine dissolved in* 1 *ml. of glacial acetic acid containing varying amounts of water. The titration was performed about* 5 *minutes after the sample had been dissolved. Equivalent weight found by visual macro-titration:* 144·6 (*Calc.* 143·2).

Water content:	0·02%	0·15%	0·6%	1·0%
	164·2	152·0	148·8	148·6
	162·4	153·1	147·6	147·8
			147·9	147·6
			Av. 148·1	Av. 148·0

We conclude that Fritz and Keen's procedure cannot be used safely unless the water content of the glacial acetic acid is controlled. In our procedure a water content of 0·75% is employed for titration of primary aromatic amines.

In the titration of the hydrohalides of primary aromatic amines 100 μl. of 0·02M-mercuric acetate in glacial acetic acid [1] must be added. Consequently the sample is dissolved in 0·3 ml. of glacial acetic acid (1·0% H_2O) to obtain a final water concentration of 0·75%.

As it is not possible to obtain accurate visual titrations in glacial acetic acid containing more than 0·2% of water because of the indefinite nature of the colour change at the end-point and the complicated relationship between ionic strength and indicator equilibrium, these titrations were done potentiometrically. Table 4 shows that in a medium

[8] Ekeblad, *J. Pharm. Pharmacol.*, 1952, **4**, 636.
[9] Beckett and Tinley, "Titration in Non-Aqueous Solvents," B.D.H. Ltd., Poole, England, 1955.
[10] Keen and Fritz, *Analyt. Chem.*, 1952, **24**, 564.

TABLE 4.

Compound (M.W.)	Equiv. found in acetic acid containing the following percentages of water: 0·02	0·15	0·75	1·5	Equiv. by macro-titration
p-Anisidine (123·1)	136·4 139·7	130·9 131·2	127·0 * Max. error 4·4 Min. error 3·3	126·0 * Max. error 4·3 Min. error 2·6	124·8
1-Naphthylamine (143·2)	—	—	148·3 ‡ Max. error 5·8 Min. error 4·2	148·7 149·4	144·6
p-Anisidine hydrochloride (159·6)	—	—	163·8 ‡ Max. error 6·5 Min. error 2·4	—	161·2

Average of 8 determinations *, 4 determinations †, 5 determinations ‡.

containing 0·75% of water an accuracy of 1—3% is obtainable. The higher limit of error is undoubtedly due to the slight acetylation which still occurs. This argument is consistent with our observation that amongst some fifty titrations of primary aromatic amines on the submicro-scale we have never obtained an equivalent weight less than that obtained on the macro-scale where the acetylation effect is not noticeable.[11,12]

The presence of 0·75% of water in the solvent adversely affects the nature of the potential break at the end-point. To obtain a reasonable curve it is advisable near the end-point to add the titrant in increments of 2 μl. rather than the customary 1 μl.

EXPERIMENTAL

Titration of Bases.—Reagents. 0·01N-Sodium acetate prepared by dissolution of *ca.* 1·36 g. of "AnalaR" sodium acetate trihydrate in glacial acetic acid,[1] and made up to 1 l. This solution was standardised by titrating measured portions of 0·01N-perchloric acid in acetic acid with it as described previously.[1] A blank determination was made and the above titre corrected accordingly. A normality must be calculated for potentiometric and visual-indicator titrations. Other reagents were as described previously.[1] The apparatus was as described before.[1]

Procedure (Back titration). The weighed sample (50—60 μg.) was placed in the titration vessel and 0·4 ml. of glacial acetic acid, 1 drop of Crystal Violet indicator, and a slight excess (*ca.* 5—8 μl.) of 0·01N-perchloric acid were added and the contents of the vessel were allowed to dissolve under magnetic stirring (3 min. for xanthates, 8—10 min. for amino-acids). A blank determination was made and deducted from the above titre.

Other procedures were as described previously.[1] The stirring time was extended to 8 min. for *S*-ethylthiuronium picrate.

Titration of Primary Aromatic Amines and their Halides.—Reagents. 0·02M-Mercuric acetate, prepared by dissolution of *ca.* 0·8 g. of solid in glacial acetic acid [1] and diluted to 250 ml. Mercuric acetate must conform to purity tests specified elsewhere.[9] Other reagents were as described previously.[1] Apparatus was as before.[1]

Procedure. The sample was dissolved in 0·4 ml. of glacial acetic acid (water content 0·75%) and the potentiometric titration was performed as described previously, except that the titrant was added in 2·0 μl. increments near the end-point. A blank analysis was determined on the same amount of solvent. In the titration of the hydrohalides the sample was dissolved in 0·3 ml. of glacial acetic acid (1·0% water content) and 100 μl. of 0·02M-mercuric acetate were added before titration.

For the titration of other amine hydrohalides and quaternary ammonium compounds, the sample was dissolved in 0·3 ml. of glacial acetic acid,[1] and 100 μl. of 0·02M-mercuric acetate were added.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
BIRMINGHAM 15.

[*Received, March 13th*, 1959.]

[11] Fritz, *Analyt. Chem.*, 1950, **22**, 1028.
[12] Markunas and Riddick, *ibid.*, 1951, **53**, 337.

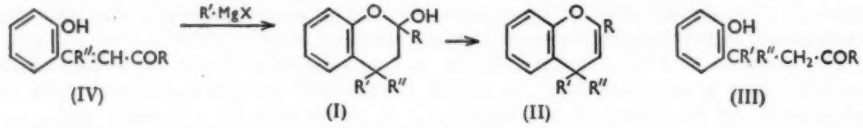
XUM

578. *The Preparation of Some Chroman Derivatives.*

By R. H. Hall and B. K. Howe.

2-Methyl-4-phenylchroman-2-ol and 2-methyl-4-phenylchrom-2-en have been prepared from salicylideneacetone and phenylmagnesium bromide. The chromanol has been degraded to 4-*o*-methoxyphenyl-4-phenylbutan-2-one, the structure of which was proved by synthesis from ethyl α-cyanocinnamate. Methylmagnesium bromide and salicylideneacetophenone gave 3′-*o*-hydroxyphenylbutyrophenone, which on dehydration afforded 4-methyl-2-phenylchrom-2-en.

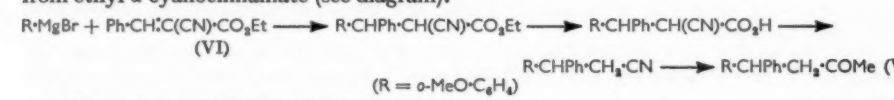
2-Methyl-4- (I; R = Me, R′ = Ph, R″ = H) and 4-methyl-2-phenyl-chroman-2-ol (I; R = Ph, R′ = Me, R″ = H) and the related chromens were required during a recent investigation.[1] This paper describes the preparation of the two chromens and of one (I; R = Me, R′ = Ph, R″ = H) of the chromanols; the other chromanol could not be obtained, the keto-phenol (III; R = Ph, R′ = Me, R″ = H) being the stable form.



Chroman-2-ols have been obtained, *inter alia*, by treatment of coumarins with Grignard reagents,[2-4] by 1,4-addition of Grignard reagents to aryl *o*-hydroxystyryl ketones [2] [although it has been claimed [5] that this gives the isomeric keto-phenols (III)], by decarbonylation of chroman-2-carboxylic acids,[6] and by alkaline hydrolysis of 3-acetyl-3,4-dihydrocoumarins.[7] The last route furnished the chromanols admixed with the isomeric keto-phenols (III) from which they could be separated by virtue of their insolubility in alkali. Both species gave the same 2,4-dinitrophenylhydrazone.

In the present investigation addition of phenylmagnesium bromide to salicylideneacetone (IV; R = Me, R″ = H) gave a mixture of 2-methyl-4-phenylchroman-2-ol and its dehydration product, 2-methyl-4-phenylchrom-2-en, which were separated by distillation. The infrared absorption spectrum of the former resembled that of 2,4,4-trimethylchroman-2-ol (I; R = R′ = R″ = Me); [6,8] in particular the absence of any appreciable bands between 1600 and 1800 cm.$^{-1}$ indicated that no carbonyl group was present and excluded the structure (III; R = Me, R′ = Ph, R″ = H). In agreement with the spectral data the compound did not give a semicarbazone. It did, however, dissolve very slowly on being shaken with aqueous alkali, from which solution it was reprecipitated unchanged (infrared) by acidification. As the infrared data indicate that not more than a trace of the keto-phenol form can be present isomerisation must occur as this dissolution in alkali takes place.

On methylating cleavage under drastic conditions (cf. refs. 6 and 8), the chromanol furnished 4-*o*-methoxyphenyl-4-phenylbutan-2-one (V) which was characterised as the 2,4-dinitrophenylhydrazone. The structure of this ketone was established by its synthesis from ethyl α-cyanocinnamate (see diagram).



[1] Howe, B.P. 796,794 (Distillers Co., Ltd.).
[2] Löwenbein, *Ber.*, 1924, **57**, 1517.
[3] Löwenbein and Rosenbaum, *Annalen*, 1926, **448**, 223.
[4] Heilbron and Hill, *J.*, 1927, 2005.
[5] Geissman, *J. Amer. Chem. Soc.*, 1940, **62**, 1363.
[6] Baker, Curtis, and McOmie, *J.*, 1952, 1774.
[7] Dean, Robertson, and Whalley, *J.*, 1950, 895.
[8] Webster and Young, *J.*, 1956, 4785.

The infrared absorption spectrum of the 2-methyl-4-phenylchrom-2-en was consistent with this formulation [in carbon tetrachloride; band in the region 1225—1250 cm.$^{-1}$ (C–O–C of alkyl aryl ether) and a sharp band at 1702 cm.$^{-1}$ (C=C of chrom-2-en; cf. 2,4,4-trimethylchrom-2-en[8] which has a band at 1704 cm.$^{-1}$)]. With bromine in carbon tetrachloride at 0° in the dark a solid dibromochroman was obtained. At room temperature hydrogen bromide was disengaged and a monobromochromen obtained (cf. refs. 6 and 8).

Brief attempts were made to convert the ketone (V) into 2-methyl-4-phenylchroman-2-ol and/or 2-methyl-4-phenylchrom-2-en by dealkylation with hydrogen bromide[9] or with boron trichloride;[10] in the former case, a low yield of an impure product containing the chromen (detected spectroscopically) was eventually obtained, but the latter reagent was ineffective. The matter was not pursued further.

Addition of methylmagnesium bromide to salicylideneacetophenone (IV; R = Ph, R″ = H) failed to give any 4-methyl-2-phenylchroman-2-ol. Instead, the product was the open-chain tautomer, 3′-*o*-hydroxyphenylbutyrophenone (III; R = Ph, R′ = Me, R″ = H), as shown by its ready solubility in alkali, formation of a semicarbazone, and infrared absorption spectrum. The spectrum contained a strong band (1665 cm.$^{-1}$ in crystalline state; 1680 cm.$^{-1}$ in chloroform) indicative of a carbonyl or ethylenic group; the absence of strong bands in the 1060—1150 cm.$^{-1}$ region excluded an alkyl aryl ether grouping. Treatment of the keto-phenol with oxalic acid caused elimination of water and production of a compound which from its method of formation, spectral properties, and behaviour towards bromine was the chromen (II; R = Ph, R′ = Me, R″ = H). Its infrared absorption spectrum (carbon tetrachloride) contained bands at 1225 cm.$^{-1}$ (C–O–C of alkyl aryl ether) and 1671 cm.$^{-1}$; the latter was assigned to the C=C of the chrom-2-en, the displacement from the more usual position around 1700 cm.$^{-1}$ being attributed to conjugation of the C=C group with the 2-phenyl group [cf. 2,4-diphenylchrom-2-en (below)]. With bromine in carbon tetrachloride at room temperature immediate decolorisation occurred and hydrogen bromide was evolved; a solid derivative could not, however, be isolated.

The above results recalled the disagreement in the literature, noted earlier, concerning the structure of 2,4-diphenylchroman-2-ol (I; R = R′ = Ph, R″ = H). Prepared originally by Löwenbein[2] and formulated by him as the chromanol, this compound was stated by Geissman[5] to be the keto-phenol (III; R = R′ = Ph, R″ = H). Re-examination has confirmed the correctness of Geissman's views: the compound dissolved, albeit slowly, in aqueous sodium hydroxide, formed a semicarbazone, and contained a carbonyl group conjugated with an aromatic ring [infrared absorption band (in chloroform) at 1683 cm.$^{-1}$]. Dehydration in boiling acetic acid (cf. ref. 2) furnished 2,4-diphenylchrom-2-en whose infrared absorption spectrum (in chloroform) contained bands at 1225 cm.$^{-1}$ (C–O–C of alkyl aryl ether) and 1672 cm.$^{-1}$ (C=C of chrom-2-en).

Generalisation from the limited number of examples available is probably of doubtful value, but nevertheless it appears that, when the group R is phenyl, compounds which theoretically can have either structure (I) or (III) exist solely as (III). Presumably the gain in delocalisation energy resulting from conjugation of the carbonyl group with the aromatic ring stabilises the keto-phenol form. When R is not phenyl (aryl) other factors such as the presence of a substituent on the carbon atom β to the potential carbonyl group appear to be important, since although the chromanol form (I) is the preferred one when R = Me, R′ = Ph, and R″ = H (see above), and when R = R′ = R″ = Me,[6,8] both forms exist when R = Me and R′ = R″ = H.[7] In the latter case, however, no spectral data are recorded, and it is conceivable that a rapid isomerisation from the chromanol to the keto-phenol form occurs under the influence of the alkali which is used to separate the isomers.

[9] Cf. Elderfield and King, *J. Amer. Chem. Soc.*, 1954, **76**, 5439.
[10] Cf. Gerrard and Lappert, *J.*, 1952, 1486.

XUM

Experimental

Reaction of Salicylideneacetone with Phenylmagnesium Bromide.—Salicylideneacetone (13·5 g.) was added to phenylmagnesium bromide prepared from magnesium (7·3 g.), a trace of iodine, and redistilled bromobenzene (44·1 g.) in ether. The red solution was refluxed for 3 hr., cooled, and poured on ice–ammonium chloride. The ether layer was decanted and the residue shaken twice more with ether. The combined ether extracts were dried (Na_2SO_4) and evaporated, and part (16·4 g.) of the semi-solid residue (18·0 g.) was distilled through a short Vigreux column. A small fore-run (1·1 g.) of diphenyl was followed by (i) *2-methyl-4-phenylchrom-2-en* (8·5 g., 50%), b. p. 115—117°/0·3—0·4 mm., n_D^{20} 1·6032 (Found: C, 86·55; H, 6·35. $C_{16}H_{14}O$ requires C, 86·45; H, 6·35%), and (ii) *2-methyl-4-phenylchroman-2-ol* (3·2 g., 18%), b. p. 138—160°/0·3 mm., m. p. 116° [from light petroleum (b. p. 100—120°)] (Found: C, 80·2; H, 6·75. $C_{16}H_{16}O_2$ requires C, 79·95; H, 6·7%).

Repetition of the condensation in the absence of iodine resulted in a higher yield (25%) of chromanol. Little chromen was obtained. Both preparations afforded considerable quantities of very high-boiling residues.

Reactions of 2-Methyl-4-phenylchrom-2-en.—(*a*) Bromine (0·80 g.) in carbon tetrachloride (5 ml.) was added to the chromen (1·11 g.) in carbon tetrachloride (10 ml.) at 0° in the dark during 30 min. After a further 15 min. the solution was concentrated to about one-half of its bulk and then kept overnight at room temperature. Treatment with charcoal and evaporation *in vacuo* afforded a gum which was dissolved in light petroleum (b. p. 40—60°). Crystals (0·95 g.) slowly separated from this solution at 3°. Recrystallisation from the same solvent afforded *2,3-dibromo-2-methyl-4-phenylchroman*, m. p. 110° (Found: C, 50·1, 50·25; H, 3·6, 3·6; Br, 42·1. $C_{16}H_{14}OBr_2$ requires C, 50·3; H, 3·7; Br, 41·85%). The infrared absorption spectrum contained no bands near 1680—1700 $cm.^{-1}$, indicating absence of C=C groups.

(*b*) On bromination at room temperature hydrogen bromide was evolved. Isolation of the product afforded a small yield of a solid, m. p. 145° (from ethanol). Analysis indicated that this was impure monobromochromen (Found: Br, 24·0. Calc. for $C_{16}H_{13}OBr$: Br, 26·55%).

Reactions of 2-Methyl-4-phenylchroman-2-ol.—(*a*) No semicarbazone could be prepared from the chromanol.

(*b*) When the chromanol (1 g.) was shaken with excess of N-sodium hydroxide for 72 hr., part (0·55 g.) of it remained undissolved. This was filtered off and the filtrate was acidified. Isolation of the product with ether afforded a crude solid, m. p. 109°, whose infrared absorption spectrum was virtually identical with that of the starting material.

(*c*) The chromanol (2 g.), sodium hydroxide (40 g.), and water (50 ml.) were refluxed for 15 min. and, as some oil remained undissolved, methanol (10 ml.) was added and refluxing continued for 30 min. The product was cooled and dimethyl sulphate (25 ml.) in methanol (25 ml.) added slowly (10 min.). The mixture was then refluxed for 15 min., cooled, and diluted with water (200 ml.). Isolation of the product with ether (2 × 50 ml.) afforded an oil (1·84 g.) which readily solidified. Recrystallisation from ethanol gave 4-*o*-methoxyphenyl-4-phenylbutan-2-one, m. p. 83°, identical (mixed m. p.) with that obtained below. The 2,4-dinitrophenylhydrazone separated from ethanol as yellowish-orange needles, m. p. and mixed m. p. with authentic material (see below) 166—167° (Found: C, 63·6; H, 5·15; N, 12·5. Calc. for $C_{23}H_{22}O_5N_4$: C, 63·6; H, 5·1; N, 12·9%).

Ethyl α-Cyano-β-o-methoxyphenyl-β-phenylpropionate.—Ethyl α-cyanocinnamate (129·3 g.; prepared in 85% yield from benzaldehyde and ethyl cyanoacetate by the procedure of Baker and Leeds [11]) was added at 5° to *o*-methoxyphenylmagnesium bromide prepared from magnesium (19·4 g.) and *o*-bromoanisole (149·6 g.) in ether containing a trace of iodine. An exothermic reaction ensued and the Grignard complex separated as a thick, viscous oil. The mixture was refluxed for 1 hr., cooled, and decomposed by addition of ice-cold 5% sulphuric acid (800 ml.). The thick oil gradually disappeared with evolution of heat. The ether layer was separated, washed successively with water, 5% aqueous sodium carbonate solution, and water, and dried ($CaCl_2$). The ether was removed *in vacuo* and the residue distilled. The distillate (174·3 g.), b. p. 180°/0·4 mm., slowly crystallised. Repeated recrystallisations from 95% ethanol furnished *ethyl α-cyano-β-o-methoxyphenyl-β-phenylpropionate* (88%), m. p. 91·5—92° (Found: C, 74·1; H, 6·25; N, 4·5. $C_{19}H_{19}O_3N$ requires C, 73·75; H, 6·2; N, 4·55%).

[11] Baker and Leeds, *J.*, 1948, 974.

α-Cyano-β-o-methoxyphenyl-β-phenylpropionic Acid.—Ethyl α-cyano-β-*o*-methoxyphenyl-β-phenylpropionate (61·9 g.) was added to sodium hydroxide (21·7 g.) dissolved in water (630 ml.) at about 90°. The mixture was heated to boiling (5 min.) and refluxed for 5 min., by which time all the oil had reacted. The solution was cooled, diluted with water (600 ml.), extracted with ether (3 × 100 ml.) to remove neutral materials, then acidified with 10% hydrochloric acid and again extracted with ether (3 × 150 ml.). The combined ether solutions from this last extraction were dried (Na_2SO_4) and evaporated *in vacuo*. The oil obtained slowly solidified. Recrystallisation from benzene afforded *α-cyano-β-o-methoxyphenyl-β-phenylpropionic acid* (56 g., 100%), m. p. 132° (Found: C, 72·8; H, 5·4; N, 5·1%; equiv., 282·0. $C_{17}H_{15}O_3N$ requires C, 72·6; H, 5·4; N, 5·0%; equiv., 281·3).

β-o-*Methoxyphenyl-β-phenylpropionitrile.*—α-Cyano-β-*o*-methoxyphenyl-β-phenylpropionic acid (51·3 g.) was heated at 190° for 30 min. to effect decarboxylation. Part (41·85 g.) of the product (44·0 g.) was carefully fractionated to give a colourless distillate (30·6 g., 74%), b. p. mainly 175°/0·7 mm., which readily solidified. A solution of the solid in chloroform was washed with sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated under reduced pressure. The product obtained was recrystallised from ethanol to give β-o-*methoxyphenyl-β-phenylpropionitrile*, m. p. 90·5—91° (Found: C, 80·75; H, 6·2; N, 5·8. $C_{16}H_{15}ON$ requires C, 80·95; H, 6·35; N, 5·9%).

4-o-*Methoxyphenyl-4-phenylbutan-2-one.*—A suspension of β-*o*-methoxyphenyl-β-phenylpropionitrile (47·5 g.) in ether (200 ml.) was added to stirred methylmagnesium bromide prepared from methyl bromide and magnesium (14·6 g.) in ether (200 ml.). The exothermic reaction which ensued during the addition was controlled by external cooling and the final mixture was refluxed for 3 hr. Ice (240 g.) was added cautiously and the mixture was set aside overnight. The ether-soluble material was separated off and, after isolation, was boiled with 4% sulphuric acid (200 ml.) for 30 min. The material insoluble in ether was similarly treated with 4% sulphuric acid (265 ml.) and the products from the two hydrolyses were combined and isolated with ether. The dark brown solid (45·5 g., 89%), m. p. 75—80°, thus obtained was crystallised from ethanol (charcoal) to give 4-o-*methoxyphenyl-4-phenylbutan-2-one*, m. p. 83·5—84° (Found: C, 80·2; H, 7·1. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·15%). The *2,4-dinitrophenylhydrazone* separated from ethanol as yellowish-orange needles, m. p. 167° (Found: C, 63·85; H, 5·0; N, 12·6. $C_{23}H_{22}O_5N_4$ requires C, 63·6; H, 5·1; N, 12·9%).

De-alkylation of 4-o-*Methoxyphenyl-4-phenylbutan-2-one.*—A mixture of the ketone (10 g.) and a ~50% solution (350 ml.) of hydrobromic acid in acetic acid was refluxed for 15 hr. under nitrogen. Most (260 ml.) of the solvent was distilled off, the residue was diluted with water (300 ml.), and the mixture was extracted with ether (2 × 250 ml.). The combined ether extracts were washed successively with water, 2·5% aqueous sodium carbonate, and water, dried (Na_2SO_4), and evaporated *in vacuo*. The red oily residue (8·9 g.) was chromatographed in benzene (15 ml.) over alumina (40 × 2 cm.). The column was washed with benzene. Evaporation of the first 500 ml. of effluent gave a red oil (6·2 g.) which was fractionated under reduced pressure. Only the first fraction (0·9 g.), b. p. 137—139°/0·35—0·4 mm., contained a detectable amount of 2-methyl-4-phenylchrom-2-en; the overall yield of the latter from the ketone was estimated by infrared spectrography to be about 3%. The higher-boiling fractions from the distillation contained some unchanged ketone and some unidentified material.

Reaction of Salicylideneacetophenone with Methylmagnesium Bromide.—Salicylideneacetophenone (44·8 g.) was added gradually to a stirred, refluxing ethereal solution of methylmagnesium bromide prepared from methyl bromide and magnesium (14·65 g.). The mixture was refluxed for 3 hr., cooled, and poured on ice and ammonium chloride. The aqueous phase was acidified with concentrated sulphuric acid (55 g.) to dissolve magnesium compounds and extracted with ether. The combined ether solutions were dried (Na_2SO_4–Na_2CO_3) and evaporated *in vacuo*. The residue was distilled. Most of the distillate had b. p. 173—173·5°/0·6 mm. and slowly crystallised. Recrystallisation from benzene–light petroleum (b. p. 100—120°) afforded 3′-o-*hydroxyphenylbutyrophenone* (37·2 g., 77·5%), m. p. 80—81° (Found: C, 80·25; H, 6·7. $C_{16}H_{16}O_2$ requires C, 79·95; H, 6·7%).

4-*Methyl-2-phenylchrom-2-en.*—3′-*o*-Hydroxyphenylbutyrophenone (10 g.), oxalic acid (0·2 g.), and benzene (50 ml.) were refluxed for 3 hr. under a Dean and Stark head to effect dehydration. The cooled benzene solution was washed with water (3 × 30 ml.), dried (Na_2SO_4), and evaporated *in vacuo*. The residue was fractionated to give 4-*methyl-2-phenylchrom-2-en* (7·6 g.,

XUM

82%), b. p. 109°/0·1 mm., n_D^{20} 1·6117 (Found: C, 86·75; H, 6·35. $C_{16}H_{14}O$ requires C, 86·45; H, 6·35%).

Reaction of Salicylideneacetophenone with Phenylmagnesium Bromide.—Löwenbein's procedure [2] was employed. Recrystallisation of the crude product from benzene afforded 3′-*o*-hydroxyphenyl-3′-phenylpropiophenone, m. p. 165° (Found: C, 83·8; H, 6·0. Calc. for $C_{21}H_{18}O_2$: C, 83·4; H, 6·0%). Löwenbein [2] gives m. p. 165—166° for his product; Geissman [1] gives m. p. 167—167·5°. This ketone dissolved slowly on being shaken with an excess of aqueous N-sodium hydroxide.

The ketone gave a semicarbazone (with some difficulty), which on recrystallisation from dilute ethanol had m. p. 177° (Found: N, 11·85. Calc. for $C_{22}H_{21}O_2N_3$: N, 11·7%). Geissman [1] records m. p. 177—178°.

Dehydration of the ketone with boiling acetic acid (cf. ref. 2) afforded 2,4-diphenylchrom-2-en which separated from light petroleum (b. p. 60—80°) as white prisms, m. p. 109° (Found: C, 89·0; H, 5·55. Calc. for $C_{21}H_{16}O$: C, 88·7; H, 5·65%). Löwenbein [2] gives m. p. 110°.

The authors are indebted to Miss M. M. R. Gay-Knott and Miss P. E. Joyce for assistance with the experimental work and to Messrs. A. R. Philpotts, W. Maddams, and W. R. Ward for infrared data.

Research and Development Department,
The Distillers Co. Ltd., Great Burgh, Epsom, Surrey. [*Received, March 26th*, 1959.]

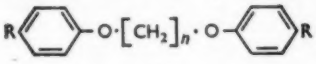
---

579. *Synthesis of Bis-*[p-*di*-(2-*chloroethyl*)*aminophenoxy*]*alkanes.*

By F. Bergel and E. Reiner.

A homologous series of compounds based on the structure mentioned in the title has been prepared from the corresponding primary diamines *via* the hydroxyethylamino-derivatives.

In recent years, attention of a number of research teams has centred on schistosomicidal drugs derived from diphenoxyalkanes, particularly those (I) substituted in the *p*-positions with primary, secondary, and tertiary amino-groups.[1-3] This structure has served as a basis for our synthesis of a homologous series, carrying two "nitrogen mustard" groups [I; R = $(Cl{\cdot}CH_2{\cdot}CH_2)_2N$; n = 2—10 and 12]. We were hoping to find differences in biological behaviour with variations in polymethylene chain length; in the literature examples of such variations have been reported in relation to pharmacodynamic,[4,5] enzymic,[6] anti-protozoal,[7] as well as anti-tumour [8] and anti-leukæmic [9] properties.



(I)

Starting materials were αω-polymethylene dibromides and *p*-nitrophenoxide (formed *in situ* from *p*-nitrophenol and anhydrous potassium carbonate) which, in ethyl methyl ketone and in presence of potassium iodide,[10] gave the dinitro-compounds in high yields (I; R = NO_2; n = 1—12). Of these, some have been reported with analyses in the

[1] Raison and Standen, (*a*) *Trans. Roy. Soc. Trop. Med. Hyg.*, 1954, **48**, 446; (*b*) *Brit. J. Pharmacol.*, 1955, **10**, 191.
[2] Collins, Davis, and Hill, *Chem. and Ind.*, 1954, 1072.
[3] Ashley, Collins, Davis, and Sirett, *J.*, 1958, 3298.
[4] Barlow and Ing, *Brit. J. Pharmacol.*, 1948, **3**, 298.
[5] Paton and Zaimis, *ibid.*, 1949, **4**, 381.
[6] Blaschko and Duthie, *Biochem. J.*, 1945, **39**, 347.
[7] King, Lourie, and Yorke, *Ann. Trop. Med. Parasit.*, 1938, **32**, 177.
[8] Kon and Roberts, *J.*, 1950, 978.
[9] Haddow and Timmis, *Lancet*, 1953, I, 207.
[10] Everett, "Recent Advances in the Field of Chemotherapy of Cancer," Dissertation presented in support of Application for Fellowship, Royal Inst. of Chem., 1955, p. 215.

literature;[11] the others have been quoted with incomplete data in patents[12a,b,c] and are presented in Table 1. The dinitro-compounds were catalytically reduced to the corresponding diamines (I; R = NH_2; n = 1—12) of which those not previously recorded in full[3,10,11,12b,c] or only described as salts or derivatives of the free bases[3] are assembled in Table 2. Interaction with ethylene oxide in aqueous acetic acid[13] produced the bis-[di-(2-hydroxyethyl)amino]-derivatives [I; R = $(HO{\cdot}CH_2{\cdot}CH_2)_2N$; n = 1—12]. Of these (Table 3), the C_2 and C_3 analogues have been described by Everett[10] and some of the others have been mentioned with m. p. only in patents.[12c,d] The hydroxyethyl derivatives, with the exception of the compounds (I; n = 1 and 11), were in turn transformed into " nitrogen mustard " compounds (Table 4).

In view of maximum schistosomicidal activities of the corresponding amino-derivatives (I; R = Me_2N; n = 3—8)[10] three compounds [I; R = $(Cl{\cdot}CH_2{\cdot}CH_2)_2N$; n = 2, 6, 7] were tested on the Walker rat carcinoma 256. Of these the C_7 compound (CB 3214) at 500 mg./kg. (non-toxic dose) produced a slight hold-up of the tumour but the C_6 analogue (CB 3139) at the same dose level showed no inhibition. In our experiments toxic effects on the retina of the animals were absent, although such effects have been reported for mainly primary diamines in carnivores and primates.[14]

Experimental.—*αω-Polymethylene dibromides.* The dibromoalkanes with one to five carbon atoms as well as decamethylene bromide were obtained from commerical sources.

Hexa- and nona-methylene dibromides were prepared from their respective glycols.[15] Pimelic ester was reduced with lithium aluminium hydride[16] to its glycol which was in turn converted into the C_7 dibromide.[15] The C_8 dibromide was obtained from 1,8-dimethoxyoctane by the general method of Nineham.[17] The C_{11} dibromide (yield 69%) was prepared from the glycol which was obtained by reduction of diethyl undecanedioate.[16] The last compound was

TABLE 1. *Nitro-compounds* (I; R = NO_2).

		Yield		Found (%)			Required (%)			
n	M. p.	(%)	Formula	C	H	N	C	H	N	Ref.
5	102—104 [a]	57	$C_{17}H_{18}N_2O_6$	58·7	5·3	8·1	58·9	5·2	8·1	12*a*
6	106—108 [b]	90	$C_{18}H_{20}N_2O_6$	60·1	5·8	7·6	60·0	5·6	7·8	12*b*
7	114—116 [a]	90	$C_{19}H_{22}N_2O_6$	61·3	5·9	7·5	61·0	5·9	7·5	12*c*
11	79·5—81·5 [c]	96	$C_{23}H_{30}N_2O_6$	63·9	7·0	6·2	64·2	7·0	6·5	

Solvents: *a*, ethyl acetate; *b*, ethanol; *c*, propan-2-ol; *d*, benzene–light petroleum.

TABLE 2. *Amines* (I; R = NH_2).

		Yield		Found (%)			Required (%)			
n	M. p.	(%)	Formula	C	H	N	C	H	N	Ref.
5	80—82° [b,d]	91	$C_{17}H_{22}N_2O_2$	71·5	7·7	9·7	71·3	7·7	9·8	12*b*
6	146—147·5 [b]	94	$C_{18}H_{24}N_2O_2$	71·6	8·0	9·3	71·9	8·05	9·3	12*b*
7	78—79·5 [d]	97	$C_{19}H_{26}N_2O_2$	72·8	8·6	8·7	72·6	8·3	8·9	12*c*
11	72—74 [c]	97	$C_{23}H_{34}N_2O_2$	74·5	9·1	7·6	74·6	9·3	7·6	

[b,d] See Table 1.

synthesised from the C_9 dibromide and sodium cyanide as described by Chuit[18] with subsequent hydrolysis and esterification. The C_{12} dibromide was obtained either by catalytic reduction

[11] Weddige, *J. prakt. Chem.*, 1880, **21**, 127; Kinzel, *Arch. Pharm.*, 1898, **236**, 260; Wilson and Baker, *J.*, 1931, 1765; Partridge and Short, *J.*, 1947, 391; McMillan, *J. Amer. Chem. Soc.*, 1952, **74**, 5229; Wagner, *J. prakt. Chem.*, 1883, **27**, 206.

[12] (*a*) B.P. 758,382/1956; (*b*) B.P. 749,923/1956; (*c*) B.P. 761,888/1956; (*d*) B.P. 770,410/1957.

[13] Everett, Roberts, and Ross, *J.*, 1953, 2386.

[14] Edge, Mason, Wien, and Ashton, *Nature*, 1956, **178**, 806; Goodwin, Richards, and Udall, *Brit. J. Pharmacol.*, 1957, **12**, 468; Collins, Davis, Edge, and Hill, *ibid.*, 1958, **13**, 238.

[15] *Org. Synth.*, 1955, Coll. Vol. III, p. 227.

[16] *Org. Reactions*, 1951, **6**, 469.

[17] Nineham, *J.*, 1953, 2601.

[18] Chuit, *Helv. Chim. Acta*, 1926, **9**, 264.

XUM

of 1,12-di-*o*-methoxyphenoxydodec-6-ene followed by cleavage and bromination or by esterification of dodecanedioic acid with subsequent reduction to the glycol and bromination of the latter.

Di(p-*nitro- and -amino-phenoxy*)*alkanes.* *p*-Nitrophenol (2 equiv.), anhydrous potassium carbonate (2 equiv.), αω-polymethylene dibromide (1 equiv.), and potassium iodide (0·02 equiv.)

TABLE 3. *Di-2-hydroxyethylamino-compound* [I; R = $(HO{\cdot}CH_2{\cdot}CH_2)_2N$]

		Yield		Found (%)			Required (%)		
n	M. p.	(%)	Formula	C	H	N	C	H	N
1	143—145° [a]	86	$C_{21}H_{36}N_2O_6$	61·7	7·4	6·9	62·05	7·4	6·9
2	112·5—113·5 [b]	56	$C_{22}H_{38}N_2O_6$	62·6	7·7	6·7	62·8	7·7	6·7
3	107—109 [b, c]	71	$C_{23}H_{40}N_2O_6$	63·9	8·1	6·5	63·6	7·9	6·5
4	130—131·5 [a]	74	$C_{24}H_{42}N_2O_6$	64·1	8·2	6·4	64·3	8·1	6·3
5	113·5—115·5 [a]	58	$C_{25}H_{44}N_2O_6$	64·6	8·1	6·1	64·9	8·3	6·1
6	109·5—111·5 [a]	84	$C_{26}H_{46}N_2O_6$	65·1	8·4	5·9	65·5	8·5	5·9
7	105·5—107 [d]	82	$C_{27}H_{48}N_2O_6$	65·9	8·6	5·8	66·1	8·6	5·7
8	108—110 [a]	75	$C_{28}H_{50}N_2O_6$	66·3	8·9	5·6	66·6	8·8	5·6
9	102·5—104 [d]	56	$C_{29}H_{52}N_2O_6$	67·0	8·9	5·3	67·15	8·9	5·4
10	108—110 [d]	70	$C_{30}H_{54}N_2O_6$	67·3	9·3	5·5	67·6	9·1	5·3
11	105—106·5 [a]	64	$C_{31}H_{56}N_2O_6$	68·1	9·5	5·3	68·1	9·2	5·1
12	112—114 [a]	46	$C_{32}H_{58}N_2O_6$	68·1	9·3	5·0	68·5	9·35	5·0

Solvents: (*a*) MeOH–light petroleum; (*b*) MeOH; (*c*) water; (*d*) chloroform–light petroleum.

TABLE 4. *Di-2-chloroethylamino-compounds* [I; R = $(ClCH_2CH_2)_2N$].

		Yield		Found (%)				Required (%)				Hydrolysis
n	M. p.	(%)	Formula	C	H	N	Cl	C	H	N	Cl	(%)
2	78—79° [a]	27	$C_{22}H_{36}O_2N_2Cl_4$	53·8	5·8	5·6	28·5	53·5	5·7	5·7	28·7	—
3	51—52 [b]	26—75	$C_{23}H_{38}O_2N_2Cl_4$	54·4	6·0	5·5	27·2	54·3	5·9	5·5	27·9	50
4	99·5—100·5 [b]	61	$C_{24}H_{40}O_2N_2Cl_4$	55·3	6·2	5·2	26·4	55·3	6·2	5·4	27·2	—
5	59·5—61·5 [b]	13	$C_{25}H_{42}O_2N_2Cl_4$	56·2	6·6	5·1	26·6	56·0	6·4	5·2	26·4	70
6 *	67—69 [a]	61	$C_{26}H_{44}O_2N_2Cl_4$	56·9	6·6	5·2	26·1	56·7	6·6	5·1	25·8	77
7	48—50 [b]	45	$C_{27}H_{46}O_2N_2Cl_4$	57·9	6·7	4·7	24·8	57·4	6·7	5·0	25·1	51
8	73—74 [a]	57	$C_{28}H_{48}O_2N_2Cl_4$	58·0	6·9	5·1	24·2	58·1	7·0	4·8	24·5	36
9	52—54 [a]	36	$C_{29}H_{50}O_2N_2Cl_4$	58·8	7·2	4·7	23·8	58·8	7·5	4·6	23·5	51
10 †	75—76 [c]	25	$C_{30}H_{54}O_2N_2Cl_4$	59·6	7·4	4·7	23·0	59·4	7·3	4·6	23·4	41
12 ‡	55—56 [d]	27	$C_{32}H_{58}O_2N_2Cl_4$	60·5	7·3	4·0	22·0	60·7	7·6	4·4	22·3	—
*	140	Dipicrate	$C_{38}H_{42}O_{16}N_8Cl_4$	45·0	4·2	10·7		45·2	4·2	11·1		
†	110	Dipicrate	$C_{42}H_{50}O_{16}N_8Cl_4$	47·5	4·9	10·2		47·3	4·7	10·5		
‡	91	Dipicrate										

Solvent: (*a*) cyclohexane; (*b*) benzene–pentane; (*c*) pentane; (*d*) ethanol.

were suspended in ethyl methyl ketone, and heated under reflux with stirring for 24 hr. (cf. Everett [10]). After cooling, the mixture was extracted with benzene which was washed with water, dried (Na_2SO_4), and evaporated *in vacuo*. The compounds were purified by recrystallisation (charcoal) (Table 1), and (0·01—0·02 mole) reduced catalytically (platinum oxide; 0·1 g.) in ethyl acetate or ethyl acetate–ethanol. The free bases after recrystallisation (charcoal) were obtained as yellowish prisms or plates (Table 2).

Bis-[p-*di-*(2-*hydroxyethyl- and* 2-*chloroethyl*)*aminophenoxy*]*alkanes.* The above amines (0·01 equiv.) were shaken with chilled acetic acid–water (1 : 1) (20 ml.) and ethylene oxide (4—5 equiv.) for 3—4 hr. After being kept for a further 12 hr. the mixture was gently heated on a water-bath, and the excess of ethylene oxide removed. The remaining solution was made alkaline with ammonia solution or saturated aqueous sodium carbonate, and the usually very hydrophilic precipitate was dried and purified by crystallisation (Table 3).

Each of the tetrahydroxyethyl compounds (0·01 mol.) was suspended in benzene (20 ml.), and phosphorus oxychloride (1—2 ml.) was added to the refluxing mixture. After 0·5 hour's heating on the water-bath most of the solvent was removed *in vacuo*, and further phosphorus oxychloride (15 ml.) added to the residue. The solution was gently heated for 5—8 hr., then the solvent was removed *in vacuo*. Treatment with concentrated hydrochloric acid on the water-bath for 3 hr. was followed by addition, with cooling, of concentrated aqueous sodium acetate and concentrated aqueous ammonia until the pH was *ca.* 6·5. The aqueous solution was extracted with benzene, and the benzene extract dried (Na_2SO_4) and concentrated *in vacuo*.

After addition of pentane (5—10 vol.) and cooling, crystals were formed. They were sensitive to sunlight but appeared quite stable in the dark (Table 4). The C_2 compound has been described by Everett.[10] Hydrolysis was measured by Ross's method.[19]

We thank Professor A. Haddow, F.R.S., for the biological results and Dr. H. J. Barber of May and Baker Laboratories for kindly supplying the 1,12-di-*o*-methoxyphenoxydodec-6-ene. This investigation was supported by grants to this Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

CHESTER BEATTY RESEARCH INSTITUTE,
INSTITUTE OF CANCER RESEARCH: ROYAL CANCER HOSPITAL,
FULHAM ROAD, LONDON, S.W.3. [*Received, April 4th*, 1959.]

[19] Ross, *J.*, 1949, 183.

---

580. *Chemical Studies in the Biosynthesis of Purine Nucleotides. Part III.*[1] *The Synthesis of 5-Amino-1-(β-D-ribofuranosyl)glyoxaline-4-carboxyamide and 4-Amino-1-(β-D-ribofuranosyl)glyoxaline-5-carboxyamide.*

By J. BADDILEY, J. G. BUCHANAN, F. E. HARDY, and J. STEWART.

The ribosyl derivative (III) of 5-aminoglyoxaline-4-carboxyamide, indistinguishable from the natural material, has been synthesised by condensing the silver or chloromercury salt of methyl 5-nitroglyoxaline-4-carboxylate (VII) with tri-*O*-benzoylribofuranosyl chloride, treatment with ammonia, separation of the resulting isomers (XIV and XVI; R = ribofuranosyl), and hydrogenation.

The isomers were oriented by comparison of their spectra with authentic methylated nitro-amides (XIV and XVI; R = Me) and amino-amides (XVII and XVIII; R = Me). An unusual rearrangement was noted during this work.

The preparation and properties of glucosyl derivatives of 4-nitro-5-styrylglyoxaline (V) were investigated. A preliminary account of this work has been published.[2]

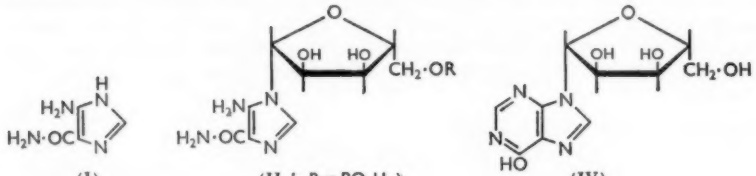
IT was observed by Stetten and Fox [3] that a base, subsequently identified [4] as 5-aminoglyoxaline-4-carboxyamide (I), accumulated during sulphonamide-inhibition of *Escherichia coli*. It was suggested [4] that the base was an intermediate in purine biosynthesis in *E. coli*. Later work showed that the carboxyamide (I) was not on the direct pathway,[5] and that the ribose phosphate derivative [6] (II) was the true precursor. Greenberg and Spilman [7] isolated the ribofuranosyl derivative (III) from sulphonamide-inhibited *E. coli*, and examined its structure. Acid-hydrolysis gave the base (I) and ribose, while formylation and ring-closure gave inosine (IV). A chemical synthesis of (III) was clearly of interest.

We envisaged a synthesis by reaction of the mercury or silver salt of a suitable glyoxaline with a tri-*O*-acylribofuranosyl halide. The carboxyamide (I) has been synthesised by a number of methods [8-10] and is readily available. It is, however, unstable to heat and to

[1] Part II, Baddiley, Buchanan, Hodges, and Prescott, *J.*, 1957, 4769.
[2] Baddiley, Buchanan, and Stewart, *Proc. Chem. Soc.*, 1957, 149.
[3] Fox, *Proc. Soc. Expt. Biol. Med.*, 1942, **51**, 102; Stetten and Fox, *J. Biol. Chem.*, 1945, **161**, 333.
[4] Shive, Ackermann, Gordon, Getzendaner, and Eakin, *J. Amer. Chem. Soc.*, 1947, **69**, 725.
[5] Cf. Baddiley and Buchanan, *Ann. Reports*, 1957, **54**, 329.
[6] Gots, *Nature*, 1953, **172**, 256.
[7] Greenberg and Spilman, *J. Biol. Chem.*, 1956, **219**, 411.
[8] Windaus and Langenbeck, *Ber.*, 1923, **56**, 683.
[9] Shaw and Woolley, *J. Biol. Chem.*, 1949, **181**, 89.
[10] Cook, Heilbron, and Smith, *J.*, 1949, 1440.

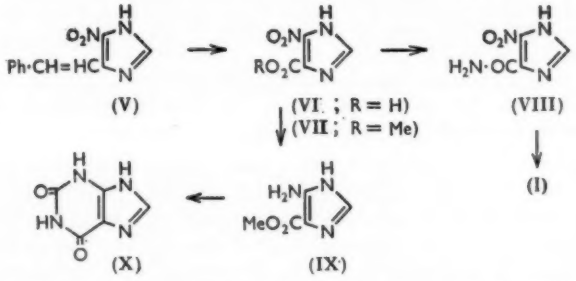
XUM

oxidation, and the presence of the amino-group is clearly undesirable in a reaction of this kind. On the other hand, protection of the amino-group by acylation yields derivatives very susceptible to cyclisation, giving xanthine or 2-substituted hypoxanthines under basic conditions.[9] For these reasons we turned to the 4-nitroglyoxalines.



(I) (II ; R = PO_3H_2) (III ; R = H) (IV)

Windaus and Langenbeck [8] prepared 4-nitro-5-styrylglyoxaline (V) and converted it into the nitro-acid (VI), the methyl ester (VII), and the amide (VIII). The ester and amide could be reduced catalytically to the corresponding amino-compounds (IX) and (I) and characterised as hydrochloride or picrate. Allsebrook, Gulland, and Story [11] sought to use some of these intermediates in a synthesis of xanthine and its glucosides. Although they successfully converted the amino-ester (IX) into xanthine (X), they were unsuccessful in attempts to convert any of the glyoxalines (V), (VII), or (VIII) into glucosyl derivatives by the use of silver salts and tetra-*O*-acetyl-α-D-glucopyranosyl bromide. In model experiments using methyl iodide in place of the glucosyl bromide methylated glyoxalines were obtained. The orientation of these products was used to predict which of the nitroglyoxalines might yield glycosyl derivatives correctly oriented for conversion into 9-glycosylpurines. We considered that a reinvestigation of these reactions, using silver or chloromercury salts [12] and tri-*O*-benzoylribofuranosyl chloride,[12,13] might lead to 5-amino-1-(β-D-ribofuranosyl)glyoxaline-4-carboxyamide (III).

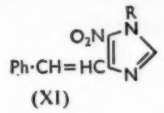


(V) (VI ; R = H) (VII ; R = Me) (VIII) (I) (X) (IX)

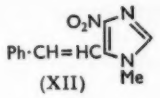
The earlier work indicated that the nitro-styrylglyoxaline (V) might give glycosyl derivatives of the correct orientation. It was found, however, that methylation of either the mercury or silver salt gave two products. One was the 1-methyl-5-nitro-derivative (XI; R = Me) as described by Allsebrook *et al.*[11] and the other the 1-methyl-4-nitro-compound (XII), originally made from 1,5-dimethyl-4-nitroglyoxaline.[11] These compounds were separated on alumina and their ultraviolet spectra were sufficiently different for use in the orientation of possible glycosyl compounds by the classical method of Gulland, Holiday, and Macrae.[14] When tri-*O*-acetyl-β-D-xylosyl bromide [15] was condensed with the silver salt of the nitro-compound (V) the triacetate of the xylosyl derivative was isolated

[11] Allsebrook, Gulland, and Storey, *J.*, 1942, 232.
[12] Haynes and Newth, *Adv. Carbohydrate Chem.*, 1955, **10**, 207.
[13] Kissman, Pidacks, and Baker, *J. Amer. Chem. Soc.*, 1955, **77**, 18.
[14] Gulland, Holiday, and Macrae, *J.*, 1934, 1639.
[15] Günther, Helferich, and Pigman, *Ber.*, 1939, **72**, 1953.

in 51% yield. Deacetylation yielded the free xyloside, whose absorption spectrum showed it to be the 5-nitro-1-xylosyl derivative (XI; R = β-D-xylopyranosyl) (see Table 1). The



(XI)



(XII)

xyloside is very labile towards acid, owing no doubt to the presence of the nitro-group, and the spectrum at an acid pH had to be measured rapidly.

TABLE 1. *Ultraviolet spectra of nitro-styrylglyoxalines in* 3 : 1 *ethanol–water.*

Glyoxaline derivative	$\lambda_{max.}$ (mμ)		ε	
	pH > 10	pH < 1	pH > 10	pH < 1
4-Nitro-5-styryl (V)	280·5	269·5	24,760	21,240
	408	371	16,860	17,400
1-Methyl-5-nitro-4-styryl (XI; R = Me)	274	273·5	18,790	22,950
	384	384	10,710	16,160
1-Methyl-4-nitro-5-styryl (XII)	268	269	19,320	23,430
	367	366	12,320	12,840
5-Nitro-4-styryl-1-xylosyl (XI; R = xylosyl)	273	273	21,820	22,020
	384	384	15,900	17,910
5-Nitro-1-ribosyl-4-styryl (XI; R = ribosyl)	273·5	270	21,480	18,830
	385	372	14,980	15,190

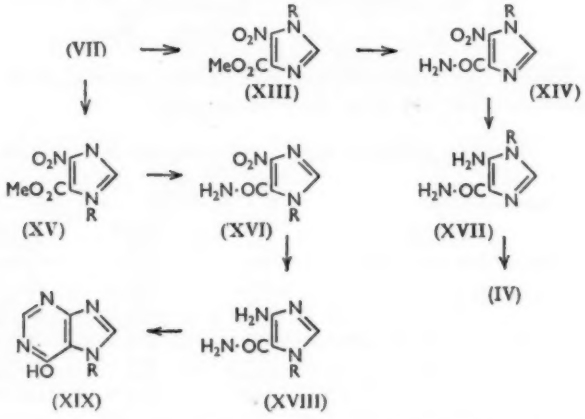
A similar reaction using tri-*O*-benzoylribofuranosyl chloride [3] was unsuccessful, but with the chloromercury salt a crystalline product was isolated after chromatography. Debenzoylation gave the ribosyl derivative (XI; R = β-D-ribofuranosyl), identified by its absorption spectra. It will be noticed (Table 1) that the spectrum in acid is the same as that of 4-nitro-5-styrylglyoxaline rather than that of the 1-methyl-5-nitro-compound. This is due to the great lability of the ribofuranosyl derivative towards acid. The spectrum in alkali is, however, sufficient for orientation. The synthetic glycosyl derivatives were assumed, by their mode of formation, to be β-compounds and to possess the same lactol ring structure as the parent glycosyl halides.

Attempts were made to oxidise the styryl compound (XI; R = tri-*O*-benzoylribofuranosyl) to the corresponding glyoxaline-4-carboxylic acid by neutral permanganate.[8,11] Great difficulties were encountered owing to solubility problems, incomplete oxidation, and the extreme acid-lability of 1-glycosyl-nitroglyoxalines.

Gulland and his co-workers [11] assumed that methylation of the silver salt of a glyoxaline was a reliable model for glycosylation. We have shown that in the nitro-styryl series this is not so. Although the earlier workers found that methylation of the silver salt of the nitro-ester (VII) gave the 1-methyl-4-nitro-compound (XV; R = Me) as the sole product, we considered that the nitro-ester (VII) might be a suitable starting point for our purpose. Condensation between the silver or chloromercury salt of the nitro-ester (VII) and tri-*O*-benzoylribofuranosyl chloride occurred in boiling xylene. Non-glycosyl compounds were removed by chromatography of the crude product on neutral alumina. A major fraction, presumably a mixture of esters (XIII and XV; R = ribofuranosyl), gave on prolonged treatment with methanolic ammonia a mixture which was examined by paper chromatography. Two components had the required properties, giving ribose and 5-nitroglyoxaline-4-carboxyamide (VIII) on mild acid-hydrolysis. Separation of the two isomers was achieved by chromatography on thick paper sheets, counter-current distribution having failed to give a clear-cut separation. One of the isomers was crystalline, and was converted by hydrogenation into a crystalline amino-compound differing from Greenberg and Spilman's ribosyl compound; [7] these synthetic compounds are shown below to have structures (XVI and XVIII respectively; R = ribofuranosyl).

The other component, present in equal amount in the original mixture, was not

crystalline, though chromatographically pure. Hydrogenation gave an amino-compound, isolated as its crystalline picrate. The free base was indistinguishable from a sample, kindly given to us by Professor G. R. Greenberg, in R_F values, ultraviolet absorption spectra, and the colour given by the Bratton–Marshall reagents.[16]



The orientation of the isomeric aminoglyoxaline carboxyamides was established in a number of ways. Greenberg and Spilman [7] showed that their compound (III) or (XVII; R = ribofuranosyl) could be converted into inosine (IV) by formylation of the amino-group, followed by ring-closure. Both synthetic aminoglyoxalinecarboxyamide isomers were treated in this way. One gave a nucleoside having R_F values and absorption spectra identical with those of inosine, in agreement with Greenberg and Spilman, whereas the other yielded a different nucleoside. The latter has the same spectrum as 7-methylhypoxanthine [17] (XIX; R = Me) and is undoubtedly the inosine isomer (XIX; R = ribofuranosyl) (see Table 2).

TABLE 2. *Ultraviolet spectra of* 7- *and* 9-*substituted hypoxanthines in water.*

	$\lambda_{max.}$ (mμ)		
	pH < 1	pH 7	pH > 10
Hypoxanthine [17]	248	—	262
Inosine [17]	247	—	254
Product from (XVII; R = ribosyl)	248	248	252
9-Methylhypoxanthine [17]	248	—	255
7-Methylhypoxanthine [17]	250	—	261
Product from (XVIII: R = ribosyl)	252	255	263

The methylated nitro-amides (XIV [11] and XVI; [18] R = Me), and the amino-amides (XVII and XVIII; [18] R = Me) were also prepared as reference compounds. Their ultraviolet spectra were compared with those of the corresponding ribosyl derivatives and the results (see Table 3) were in complete agreement with Greenberg and Spilman's structure.[7]

Two new syntheses of the amino-carboxyamide (III) from inosine (IV) have appeared [19] since the publication of our preliminary communication.[2]

Several points of interest arose during the synthesis of the methylated glyoxalines. When the silver salt of the nitro-ester (VII) was treated with methyl iodide methyl 1-methyl-4-nitroglyoxaline-5-carboxylate (XV; R = Me) was the sole product, in agreement with

[16] Bratton and Marshall, *J. Biol. Chem.*, 1939, **128**, 537.
[17] Gulland and Holiday, *J.*, 1936, 765.
[18] Sarasin and Wegmann, *Helv. Chim. Acta*, 1924, **7**, 713.
[19] Shaw, Abs. Int. Congr. Pure Appl. Chem., Paris, 1957; *J. Amer. Chem. Soc.*, 1958, **80**, 3899; Abs. 4th Internat. Congr. Biochem., Vienna, 1958, p. 6.

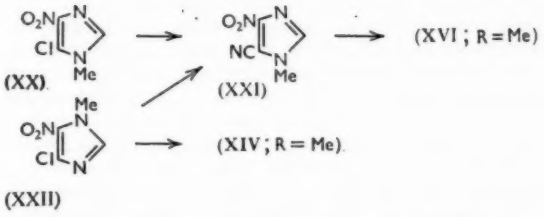
Allsebrook *et al.*[11] Treatment of this with methanolic ammonia at 0° gave the carboxyamide (XVI; R = Me) described by Sarasin and Wegmann.[18] On the other hand, by chromatography of the methylation product of the silver salt of the nitro-amide (VIII) a

TABLE 3. *Ultraviolet spectra of glyoxaline-4-carboxyamides in water.*

Glyoxaline-4-carboxyamide	$\lambda_{max.}$ (mμ) pH < 1	pH 7	pH > 10
1-Methyl-4-nitro- (XVI; R = Me)	300	299	300·5
4-Nitro-1-ribosyl- (XVI; R = ribosyl)	295	294	295·5
1-Methyl-5-nitro- (XIV; R = Me)	303·5	303·5	304·5
5-Nitro-1-ribosyl- (XIV; R = ribosyl)	304	301	301
4-Amino-1-methyl- (XVIII; R = Me)	266, 239 •	271	271
4-Amino-1-ribosyl- (XVIII; R = ribosyl)	267, 241	273	274
5-Amino-1-methyl- (XVII; R = Me)	267, 240	266·5	267
5-Amino-1-ribosyl- (XVII; R = ribosyl)	267, 247	266	267

• Shoulder.

small amount of the 5-carboxyamide (XVI; R = Me) was isolated, together with the 4-carboxyamide. Allsebrook *et al.*[11] reported the 4-carboxyamide as the sole product. We attempted to prepare the latter by an extension of Sarasin and Wegmann's method [18] for the preparation of the 5-carboxyamide (XVI; R = Me). These workers described



the reaction of 5-chloro-1-methyl-4-nitroglyoxaline (XX) with potassium cyanide in ethanol to give the cyanide (XXI) which was subsequently hydrolysed to the carboxyamide (XVI; R = Me).

When the isomeric 4-chloro-1-methyl-5-nitroglyoxaline (XXII), rigorously purified by chromatography, was treated similarly no reaction was observed. When the reactants were heated for 20 hours in dimethylformamide at 120—130° a substantial yield of the cyanide (XXI) was produced, but none of the required compound. The formation of a rearranged product is noteworthy and we are unaware of a precedent.[20] The possibility was considered that the apparent methyl migration was a result of methylation by dimethylformamide with subsequent decomposition of the quaternary compound, but the rearranged product could be isolated (in small yield) when no solvent was used. In the absence of solvent, a very small amount of 1-methyl-5-nitroglyoxaline-4-carboxyamide (XIV; R = Me) was isolated by chromatography.

Reference has been made above to the acid-lability of ribosylnitroglyoxalines. In addition, it was found during experiments on the isolation of the ribosyl derivatives of 5-nitroglyoxaline-4-carboxyamide that 5-nitro-1-ribosylglyoxaline-4-carboxyamide (XIV; R = ribosyl) was converted into the aglycone [(VIII) or (XIV; R = H)] by the action of sodium methoxide in methanol. The sugar product had the chromatographic properties of a methyl riboside. The reaction, which recalls the behaviour of an aryl glycoside [21] rather than a ribosylglyoxaline, has not been investigated further.

[20] Cf. Hofmann, " Imidazole and its Derivatives," Part I, Interscience Publ. Inc., New York, 1953.
[21] Ballou, *Adv. Carbohydrate Chem.*, 1954, **9**, 59.

XUM

Experimental

Infrared spectra were determined for potassium bromide discs.

1-Methyl-5-nitro-4-styrylglyoxaline and 1-Methyl-4-nitro-5-styrylglyoxaline.—4-Nitro-5-styrylglyoxaline (3 g.) in 50% aqueous ethanol (200 c.c.) containing sodium hydroxide (0·62 g., 1·1 mol.) was treated with mercuric chloride (4·2 g., 1·1 mol.) in the same solvent (100 c.c.) at the b. p. The yellow precipitate became orange on cooling. The salt was filtered off, washed with water, ethanol, and ether, and dried at 55° *in vacuo* (yield 6·2 g., 98%). The salt was suspended in dry, sulphur-free xylene (250 c.c.) from which 100 c.c. were removed by distillation at atmospheric pressure. Methyl iodide (6 g., 3 mol.) was added, and the mixture boiled under reflux for 2·5 hr., cooled, and evaporated to dryness. The residue was extracted (Soxhlet) with hot ethyl acetate, and the evaporated extract chromatographed from benzene on Grade 0 alumina. Two orange bands were eluted, with benzene–ether and chloroform–methanol respectively. The first gave 1-methyl-5-nitro-4-styrylglyoxaline (0·41 g.), m. p. 213—214° (from ethyl acetate) (Allsebrook *et al.*[11] give m. p. 214—215°). The second gave 1-methyl-4-nitro-5-styrylglyoxaline (0·54 g.), m. p. 143—144° (from ethyl acetate), (Found: C, 63·1; H, 4·9. Calc. for $C_{12}H_{11}O_2N_3$: C, 62·9; H, 4·8%) (Allsebrook *et al.*[11] give m. p. 150—151°).

5-Nitro-4-styryl-1-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)glyoxaline.—4-Nitro-5-styrylglyoxaline (3·3 g.) was dissolved in aqueous ethanol (1 : 2; 2·5 l.). Silver nitrate (2·5 g.) in the same solvent (50 c.c.) was added with vigorous stirring while both solutions were boiling. 6N-Ammonia was added to pH 7 and the orange precipitate of silver salt was digested at 50° for 7 hr. in the dark. After cooling, the precipitate (4·3 g., 87%) was filtered off, washed with water, ethanol, and ether, and dried *in vacuo*. Light was excluded from this product.

The silver salt (3·6 g.) was suspended in dry sulphur-free xylene (500 c.c.), and solvent (100 c.c.) was removed by distillation. The suspension was cooled, 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl bromide (3·6 g.) in xylene (100 c.c.) added, and the mixture was boiled under reflux for 0·5 hr., with stirring. Silver salts were removed by filtration, and xylene was evaporated from the filtrate under reduced pressure. The gummy residue crystallised from methanol to give the *xylosyl compound* as yellow needles (2·7 g., 51%), m. p. 149—150° (Found: C, 55·6; H, 5·4; N, 8·4. $C_{22}H_{23}O_9N_3$ requires C, 55·8; H, 4·9; N, 8·9%).

5-Nitro-4-styryl-1-β-D-xylopyranosylglyoxaline.—The above triacetate (0·32 g.) was deacetylated with methanolic ammonia (100 c.c., saturated at 0°) during 18 hr. at 0°. The solid residue obtained after evaporation was recrystallised from methanol, giving the *xylosyl derivative* as yellow needles (0·19 g., 80%), m. p. 185—187° (Found: C, 55·5; H, 5·3; N, 11·6. $C_{16}H_{17}O_6N_3$ requires C, 55·3; H, 4·9; N, 12·1%).

5-Nitro-4-styryl-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)glyoxaline.—The above mercury salt of 4-nitro-4-styrylglyoxaline (3·9 g.) with "Hyflo Supercel" silica (5 g.), was suspended in sulphur-free xylene, 100 c.c. of which were removed by distillation. To the boiling solution was added 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl chloride [from the 1-*O*-acetyl derivative (5 g.)] in xylene (100 c.c.). The mixture was boiled for 0·5 hr., then filtered while hot, and the volume of the filtrate reduced to about 50 c.c. by evaporation under reduced pressure. Addition of light petroleum (b. p. 60—80°) caused precipitation of a sticky solid, removed by filtration. The solid was treated with chloroform (150 c.c.), filtered from some 4-nitro-5-styrylglyoxaline (0·46 g.; m. p. 260—280°), and shaken with 30% potassium iodide solution, and the chloroform layer was dried ($MgSO_4$). Evaporation of the filtered solution left a gum (5 g.) which was chromatographed in benzene (100 c.c.) on neutral alumina (600 g.). A yellow band was eluted with benzene–chloroform (3 : 1), giving, from ethanol, the *ribosyl derivative* as yellow needles (2·3 g., 41%), m. p. 115—118° (Found: C, 67·8; H, 4·9; N, 6·1. $C_{37}H_{29}O_9N_3$ requires C, 67·4; H, 4·4; N, 6·4%).

5-Nitro-1-(β-D-ribofuranosyl)-4-styrylglyoxaline.—The above tribenzoate (0·3 g.) was dissolved in methanol (100 c.c.) saturated with ammonia at 0° and kept at 0° for 16 hr. The gummy residue left after evaporation of solvent was crystallised from methanol to give the *ribosyl compound* (0·16 g., 70%) as yellow needles, m. p. 255—256° (Found: C, 55·2; H, 5·4; N, 11·8. $C_{16}H_{17}O_6N_3$ requires C, 55·3; H, 4·9; N, 12·1%).

Silver Salt of Methyl 5-Nitroglyoxaline-4-carboxylate, and Condensation with Tri-O-benzoyl-ribofuranosyl Chloride.—The methyl ester [8] (1·3 g.; prepared from the acid [8,22]) was dissolved in 50% aqueous ethanol (100 c.c.) and mixed, with vigorous stirring, with a solution of silver

[22] Kuler and Gireva, *Zhur. prikład. Khim.*, 1957, **30**, 811.

nitrate (1·3 g.) in the same solvent (50 c.c.) at the b. p. The gelatinous suspension was brought to pH 7 with dilute ammonia and kept at 60° for 2 hr. " Hyflo Supercel " silica (3·6 g.) was added with shaking, and the mixture allowed to cool. Solids were filtered off, washed with water, ethanol, and ether, and then dried (P_2O_5) *in vacuo* at 50° (yield, 1·2 g., 62%). The salt was suspended in dry sulphur-free xylene, and 100 c.c. were removed by distillation at atmospheric pressure. Tri-*O*-benzoylribofuranosyl chloride [from 1-*O*-acetyl compound (4·0 g.)] in dry xylene (70 c.c.) was added and the mixture was boiled under reflux for 1 hr. with stirring. The solid was filtered off while hot, cooled, and filtered again to remove a slight opalescence. The filtrate was evaporated under reduced pressure and the gummy residue was dissolved in chloroform and then shaken with aqueous sodium hydrogen carbonate, followed by water. The chloroform solution was dried (Na_2SO_4) and evaporated to a syrup (4·35 g.) which was chromatographed in benzene on neutral alumina (250 g.). A yellow band was eluted with chloroform and gave a syrup (3·8 g.) on evaporation. The syrup was treated with methanolic ammonia (50 c.c.) at 0° for 90 hr., and evaporated to a syrup (2·7 g.), which was dissolved in a mixture of water (30 c.c.) and ethanol (10 c.c.). This solution was extracted twice with ether (5 c.c.), and the aqueous layer subjected to descending paper chromatography on sheets of Whatman No. 3 paper in solvent B. The compounds corresponding to bands at R_F 0·5 and 0·6, detected by their absorption of ultraviolet light, were extracted with water, and the solids from each isolated by freeze-drying.

The first band gave a residue (0·219 g.) which was dissolved in hot methanol, which was then filtered, and further impurities were removed by precipitation from the cold solution by addition of acetone. Solvents were removed *in vacuo* to give syrupy *5-nitro-1(β-D-ribofuranosyl)glyoxaline-4-carboxyamide* chromatographically pure (see Tables 3 and 5).

The second solid (0·244 g.) was treated similarly to remove flocculent impurities and crystallised from methanol as needles. *4-Nitro-1-(β-D-ribofuranosyl)glyoxaline-5-carboxyamide* (0·131 g.) had m. p. 175—177°, $[\alpha]_D$ −0·6° (*c* 1·02 in H_2O) (Found: C, 37·2; H, 4·8; N, 18·9. $C_9H_{12}O_7N_4$ requires C, 37·5; H, 4·2; N, 19·4%). The ribosyl derivative consumed 1·1 mol. of sodium periodate to give a dialdehyde, $[\alpha]_D$ +183·9° (*c* 1·01 in H_2O), which slowly separated from solution (see Tables 3 and 5).

5-Amino-1-(β-D-ribofuranosyl)glyoxaline-4-carboxyamide.—The above 5-nitro-compound (0·186 g.) in water (10 c.c.) was shaken with pre-reduced Adams platinum oxide (0·114 g.) in hydrogen at atmospheric pressure for 1 hr.: uptake was then complete. The catalyst was removed by filtration and the filtrate evaporated to a syrup, which was examined by paper chromatography. The major product, which absorbed ultraviolet light and behaved as a diazotisable amine, had the same R_F values as the natural compound. The syrup (0·02 g.) in water (3 c.c.) was treated at 60° with aqueous picric acid (9 c.c., saturated at 0°). After cooling, the picrate was filtered and washed with a little water. It had m. p. 213—214° (Greenberg and Spilman give no m. p.) (Found, in sample dried *in vacuo* at 70°: C, 36·8; H, 3·6; N, 19·8. Calc. for $C_{15}H_{17}O_{12}N_7$: C, 37·0; H, 3·5; N, 20·1%).

The picrate was converted into the free base by using Dowex-1 (formate) and Dowex-50 (NH_4^+) resins by Greenberg and Spilman's method. The resulting aqueous solution was freeze-dried to a white powder, $[\alpha]_D$ −50·3° (*c* 1·0 in H_2O) (Greenberg and Spilman [7] give no $[\alpha]_D$). From ethanol–water (4 : 1) crystals (0·002 g.) were obtained. R_F values are shown in Table 5 and light absorption data in Table 3.

4-Amino-1-(β-D-ribofuranosyl)glyoxaline-5-carboxyamide.—The above 4-nitro-compound (0·121 g.) in water (10 c.c.) was hydrogenated at atmospheric pressure over Adams platinum catalyst [from oxide (0·1 g.)]. After 3 hr. the catalyst was filtered off and the filtrate evaporated to small volume and finally freeze-dried. The residue crystallised from methanol as *needles* (0·05 g.), m. p. 187—189° (Found: C, 41·3; H, 5·7. $C_9H_{14}O_5N_4$ requires C, 41·9; H, 5·4%). See Tables 5 and 3 for R_F values and ultraviolet absorption data respectively.

Inosine.—The above 5-amino-compound (0·01 g.) was dissolved in 98% formic acid (1 c.c.) and treated with a mixture of acetic anhydride (0·8 c.c.) and 98% formic acid (2·3 c.c.). The mixture was warmed at 30° for 2·5 hr., then cooled to 4° for 16 hr. The solution was freeze-dried and the residue heated at 90° for 4 hr. in 0·05M-potassium hydrogen carbonate (6 c.c.). The resulting solution was examined by paper chromatography, which showed the presence of starting material and hypoxanthine, as well as inosine, identified by R_F value and ultraviolet absorption spectra (see Tables 2 and 6).

7-β-D-*Ribofuranosylhypoxanthine.*—The above 4-amino-compound (0·013 g.) was treated

in the same way as the 5-amino-compound. The products were hypoxanthine and a hypoxanthine riboside differing from inosine and having ultraviolet absorption spectra indistinguishable from those of 7-methylhypoxanthine (see Tables 2 and 6).

5-Nitroglyoxaline-4-carboxyamide.—Methyl 5-nitroglyoxaline-4-carboxylate (0·05 g.) in methanolic ammonia (50 c.c., saturated at 0°) was kept at room temperature for 4 days. Paper chromatograms showed complete disappearance of the ester. After removal of solvent, crystallisation from water gave the amide (0·038 g., 80%), m. p. 290°. Windaus and Langenbeck [8] give m. p. 291°. Similarly, methyl 1-methyl-4-nitroglyoxaline 5-carboxylate gave the amide,[18] m. p. 258—260°, in high yield.

Methylation of the Silver Salt of 5-Nitroglyoxaline-4-carboxyamide.—The silver salt was treated with methyl iodide according to Allsebrook *et al.*[11] The crude methylation product (0·8 g.) was treated with chloroform–methanol (9 : 1; 500 c.c.) and filtered. The insoluble residue was washed with dilute ammonia to dissolve any unmethylated material and recrystallised from water to give 1-methyl-5-nitroglyoxaline-4-carboxyamide (0·17 g.), m. p. 228—230°. Allsebrook *et al.*[11] give m. p. 234°. The above chloroform–methanol solution was chromatographed on Grade 0 alumina. Elution with chloroform–methanol gave first 1-methyl-4-nitroglyoxaline-5-carboxyamide with m. p. 258° after crystallisation from water. It was identified by comparison of its infrared spectrum with that of an authentic sample. Later fractions contained a mixture of 4- and 5-nitro-amide; the final fraction had m. p. 231—232° and was the pure 5-nitro-amide.

5-Amino-1-methylglyoxaline-4-carboxyamide.—1-Methyl-5-nitroglyoxaline-4-carboxyamide (0·25 g.) in water (100 c.c.) was hydrogenated over Adams catalyst (0·1 g.) until hydrogen uptake was complete. The catalyst was filtered off and the filtrate evaporated to dryness. The residue was extracted with hot ethanol from which the *amine* (0·04 g., 20%) crystallised on cooling. The pink product had m. p. 255—257°, and alcoholic solutions became red on warming [7] (Found: C, 42·4; H, 5·5; N, 40·1. $C_5H_8ON_4$ requires C, 42·8; H, 5·8; N, 40·0%).

Reactions with 4-Chloro-1-methyl-5-nitroglyoxaline and Potassium Cyanide.—In the following experiments the chloro-compound, m. p. 76—77°, had been purified by chromatography on alumina.

(*a*) When the reaction was carried out in boiling ethanol according to Sarasin and Wegmann's method [18] for the isomeric 5-chloro-compound only starting material could be isolated.

(*b*) The 4-chloro-compound (0·5 g.) was dissolved in dimethylformamide (40 g.). Potassium cyanide (0·3 g.) and potassium iodide (0·05 g.), both finely ground, were added and the mixture was heated for 20 hr. at 120—130° with continuous stirring. The dimethylformamide was distilled off under reduced pressure and the residue was shaken with chloroform (400 c.c.). The mixture was filtered, the filtrate was evaporated to dryness, and the residue crystallised from acetone–light petroleum as a pale-green solid (0·25 g.), m. p. 110—115°. After recrystallisation from methanol it had m. p. 139—140°, undepressed in admixture with authentic 5-cyano-1-methyl-4-nitroglyoxaline.[18] The infrared spectra were identical.

(*c*) The 4-chloro-compound (1·0 g.) was mixed with finely ground potassium cyanide (0·8 g.) and potassium iodide (0·1 g.) in a small Pyrex tube. The mixture was kept at 110—120° for 24 hr. with vigorous stirring and the resulting brown mass was extracted with hot chloroform (500 c.c.). Removal of solvent left a brown residue (0·88 g.) which crystallised from aqueous methanol to give starting material (0·43 g.), m. p. 75—76°. The methanolic mother-liquors were evaporated to dryness, and the residue chromatographed in benzene on Grade 0 alumina (15 g.). Elution with benzene–ether removed a further quantity of starting material, and subsequent elution with chloroform gave a yellow solid (0·035 g.) which, after recrystallisation from benzene–light petroleum and from ethanol, had m. p. 136—137°, identified as 5-cyano-1-methyl-4-nitroglyoxaline by mixed m. p. and infrared spectrum. Elution with chloroform–methanol (1 : 1) gave a yellow solid (0·03 g.), which was recrystallised from acetone–light petroleum and from water to give 1-methyl-5-nitroglyoxaline-4-carboxyamide, m. p. 231—232°, identified by infrared spectrum.

Paper Chromatography.—Unwashed Whatman No. 4 paper was used for analytical chromatograms and unwashed Whatman No. 3 for preparative work. Irrigation was normally by the ascending technique unless otherwise stated. Solvents were allowed to dry by evaporation at room temperature. The following solvent systems were used: (A) n-butyl alcohol (4)–acetic acid (1)–water (5) (upper layer); (B) ethyl acetate (5)–n-propyl alcohol (3)–water (2); (C) n-butyl alcohol (40)–ethyl alcohol (10)–water (49)–ammonia (*d* 0·88) (1) (upper layer); (D)

n-butyl alcohol (4)–water (1)–diethylene glycol (1); (E) 5% aqueous sodium dihydrogen phosphate covered by a thin layer of isopentyl alcohol.[23]

Most compounds were located by examination of the chromatogram under ultraviolet light. Glyoxalines lacking a nitro-group or a substituent on a ring-nitrogen atom reacted with the Pauly spray.[24] Free sugars were detected by aniline phthalate [25] and glycosides by the periodate–Schiff reagent spray.[26] The following modification of the Bratton–Marshall spray was used for the detection of the aminoglyoxalines: Papers were hung in a chamber filled with nitrous fumes (from sodium nitrite and acetic acid) for 5 min., removed, and sprayed with ammonium sulphamate (0·5%) in 70% aqueous ethanol. After 3 min. they were sprayed with ethanolic *N*-1-naphthylethylenediamine dihydrochloride (0·1%). The colours obtained from aromatic primary amines ranged from red to purple. The colour appeared immediately after treatment with the coupling reagent.

TABLE 4. *R_F Values of amino- and nitro-glyoxalines in solvent A.*

	R_F	Colour with Pauly reagent	Colour with B.–M. reagent
5-Nitroglyoxaline-4-carboxylic acid	0·35 *	—	—
Methyl 5-nitroglyoxaline-4-carboxylate	0·87	—	—
5-Nitroglyoxaline-4-carboxyamide	0·63	—	—
5-Aminoglyoxaline-4-carboxyamide	0·46	Blue	Purple
1-Methyl-4-nitroglyoxaline-5-carboxyamide	0·66	—	—
1-Methyl-5-nitroglyoxaline-4-carboxyamide	0·63	—	—
4-Amino-1-methylglyoxaline-5-carboxyamide	0·46	—	Purple
5-Amino-1-methylglyoxaline-4-carboxyamide	0·50	—	Purple

* Often as a double spot.

TABLE 5. *R_F Values of ribosylglyoxalines.*

	R_F in A	B	C	D	Colour with IO_4^-/Schiff reagent	B.–M. reagent
4-Nitro-1-ribosylglyoxaline-5-carboxyamide	0·45	0·60	0·44	—	Blue	—
5-Nitro-1-ribosylglyoxaline-4-carboxyamide	0·37	0·50	0·35	—	Blue	—
4-Amino-1-ribosylglyoxaline-5-carboxyamide	0·34	—	—	—	Blue	Purple
5-Amino-1-ribosylglyoxaline-4-carboxyamide	0·40	—	—	0·37	Purple	Purple

TABLE 6. *R_F Values of hypoxanthines.*

	R_F in A	E		R_F in A	E		R_F in A	E
Hypoxanthine	0·46	0·57	Inosine	0·36	0·72	7-Ribosylhypoxanthine	0·36	0·68

We thank the Nuffield Foundation for financial support. One of us (F. E. H.) acknowledges receipt of a D.S.I.R. Studentship.

KING'S COLLEGE, UNIVERSITY OF DURHAM,
NEWCASTLE UPON TYNE.

[*Received, April 13th,* 1959.]

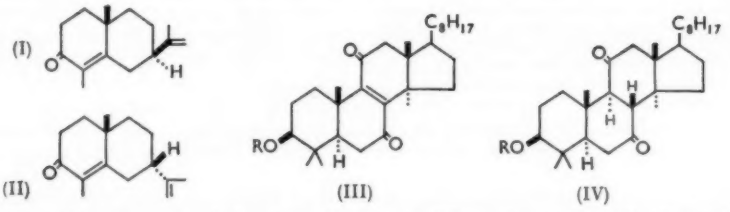
[23] Carter, *J. Amer. Chem. Soc.*, 1950, **72**, 1466.
[24] Dent, *Biochem. J.*, 1947, **41**, 240.
[25] Partridge, *Nature*, 1949, **164**, 443.
[26] Baddiley, Buchanan, Handschumacher, and Prescott, *J.*, 1956, 2818.

581. *Mechanisms of Catalytic Hydrogenation. Part I. An Examination of the Rôle of Alkali and of Acid.*

By F. J. McQuillin and W. O. Ord.

The observation [1] that alkaline conditions retard hydrogenation of the 11,12-olefinic bond in (+)-α-cyperone (I) and its $C_{(7)}$-epimer (II) in comparison with the 4,5-bond of the enone system has been extended to further examples of enones, dienones, olefins, and acetylenic compounds. The hydrogenation of the enones examined is generally unaffected by alkali or, in some cases, accelerated, whilst most of the acetylenes and olefins show retardation of reduction. Alkali promotes reduction of butyne-1,4-diol to *trans*-but-2-ene-1,4-diol. Possible reasons for these results are discussed as well as for the catalytic effect of acid.

In examining the catalytic hydrogenation of (+)-α-cyperone (I) and its $C_{(7)}$-epimer (II) in alcohol in the presence of alkali, reduction of the 11,12-olefinic bond was found to be retarded relative to that of the 4,5-bond.[1] Such differential reduction had already been noted.[2] Acid is known to catalyse and in many cases influence the steric course of hydrogenation of olefins, ketones,[3] and aromatic substances.[4]



Hydrogenations were carried out as far as possible under standardised conditions, a neutral palladised charcoal catalyst being used,[5] in a differential apparatus [6] with compensating solvent vessel. The solvent was usually ethanol or ethanolic potassium hydroxide. The ratio, rate in alkaline ethanol : rate in ethanol, was determined from the ratio of the slopes of the hydrogenation curves, which under these conditions are essentially linear for a large part of the reaction.

The rate of hydrogenation of a range of αβ-unsaturated ketones was relatively unaffected or increased by alkali, whilst the olefins examined, except styrene, showed considerable retardation, most marked with guaiazulene. Alkali catalysis of hydrogenation of the conjugated enone system is known [7] but more examples are important to show that alkali is not a catalyst poison. The lanost-8-ene-7,11-dione examples, which showed the largest alkali catalysis, were included as apparent exceptions to *cis*-hydrogen addition.[8] 7,11-Dioxolanost-8-en-3β-yl acetate (III; R = Ac) is hydrogenated directly [9] to 7,11-dioxolanostan-3β-yl acetate (IV; R = Ac).

7,11-Dioxolanost-8-en-3β-ol (III; R = H) and its acetate were reduced extremely slowly in neutral solvent, but alkali (0·5%) was strongly catalytic. In the same solvent,

[1] Howe and McQuillin, *J.*, 1958, 1194.
[2] Cf. Johnson, Bannister, Pappo, and Pike, *J. Amer. Chem. Soc.*, 1956, **78**, 6354, who give earlier references.
[3] Cf. Brewster, *ibid.*, 1954, **76**, 6361.
[4] Brown, Durand, and Marvel, *ibid.*, 1936, **58**, 1594; cf. Keenan, Giesemann, and Smith, *ibid.*, 1954, **76**, 229.
[5] Linstead and Thomas, *J.*, 1940, 1127.
[6] Jackson, *Chem. and Ind.*, 1938, **57**, 1076.
[7] Wilds, Johnson, and Sutton, *J. Amer. Chem. Soc.*, 1950, **72**, 5524; Anliker, Heusser, and Jeger, *Helv. Chim. Acta*, 1952, **35**, 838.
[8] Cf. Linstead, Doering, Davis, Levine, and Whetstone, *J. Amer. Chem. Soc.*, 1942, **64**, 1985.
[9] Dorée, McGhie, and Kurzer, *J.*, 1948, 988.

XUM

hydrogenation of the sterol and its acetate was greatly accelerated by small amounts of perchloric or acetic acid. The effect of alkali is clearly not generally catalytic (see Tables), and it appears unlikely that acid and alkali should influence the catalyst work function [10] in the same sense.

Analogous 7-oxo-8,9-olefinic steroids of the cholestane series are hydrogenated to the 8β,9α(*H*)-derivative,[11,12] whilst corresponding 11-oxo-8,9-olefinic steroids yield the 8α,9α(*H*)-derivative but much more slowly.[12] 8,9-Olefinic steroids lacking the conjugated

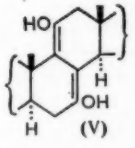
Relative rate : rate in alkaline ethanol/rate in ethanol.

(a) *αβ-Unsaturated ketones*			
Cholest-4-en-3-one	0·9	10-Ethoxycarbonyl-2-oxo-$\Delta^{1,9}$-octalin	1·0
(+)-Carvone	0·8	α-Ionone	2·2
(+)-Carvotanacetone	0·7	7,11-Dioxolanost-8-en-3β-ol *	v. large
Mesityl oxide	0·8	7,11-Dioxolanost-8-en-3β-yl acetate *	v. large
10-Methyl-2-oxo-$\Delta^{1,9}$-octalin	1·3	Sodium anthraquinone-2-sulphonate †	1·0
(b) *Acetylenes*			
Propargyl alcohol	0·3	1-Ethynylcyclohexan-1-ol	1
Butyne-1,4-diol	0·2	Phenylacetylene	0·7
Pent-2-yne-1,4-diol	0·2	Potassium acetylenedicarboxylate †	0·4
(c) *Olefins*			
Allyl alcohol ‡	0·12	Styrene ‡	0·6
Butene-1,4-diol ‡	0·07	(−)-Dihydrocarvone	0·14
Pent-2-ene-1,4-diol ‡	0·07	Hexa-2,4-diene-1-ol	0·18
1-Vinylcyclohexan-1-ol ‡	0·11	Guaiazulene	0
(d) *More conjugated ketones*			
Benzylideneacetone	0·5	3,4-Methylenedioxybenzylideneacetone	0·13
p-Dimethylaminobenzylideneacetone	0·3	*p*-Hydroxybenzylideneacetone	0·2
p-Chlorobenzylideneacetone	0·3	(+)-β-Cyperone	0·2
p-Methoxybenzylideneacetone	0·2	β-Ionone	0·2

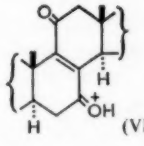
* In dioxan–ethanol (3 : 1). † In water.

‡ These figures represent the rate of the second stage of reduction of the corresponding acetylene of table (*b*).

carbonyl group are resistant to hydrogenation.[9,13] 8α,9α-Hydrogen addition leads to chair ⟶ boat compression of the molecule.[11] Isolation of the 8β,9α(*H*)-dihydro-derivative in the 7-oxo-series has been ascribed to enolisation inversion following reduction,[11] or to reduction *via* an enol.[12] Inversion following hydrogenation will not relieve compression at the reduction stage associated with 8α,9α-hydrogen addition, and alkali stabilisation of the dienol (V) or dienolate ion offers a more reasonable explanation of alkali



(V)



(VI)

catalysis in the present case. The formal analogy [14] led us to include sodium anthraquinonesulphonate in Table (a). Similarly the acid catalysis is consistent [3] with reduction *via* the conjugate acid, *e.g.* (VI).

Hydrogen-ion catalysis appeared also to be implicated in the behaviour of the benzylidene derivatives in Table (d). Those in alcohol absorbed up to 1·5 mols. of hydrogen to give mixed products showing hydroxyl absorption in the infrared region, but in presence of

[10] Cf. Dowden, *J.*, 1951, 242.
[11] Bladon, Henbest, Jones, Lovell, Wood, Woods, Ilks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921.
[12] Djerassi, Fricke, Rosenkranz, and Sondheimer, *J. Amer. Chem. Soc.*, 1953, **75**, 2496.
[13] Cf. Barton and Cox, *J.*, 1949, 214.
[14] Cf. Michaelis and Schubert, *Chem. Rev.*, 1938, **22**, 437.

XUM

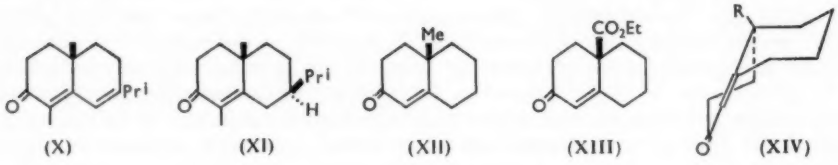
alkali absorption of hydrogen stopped at 1 mol. to give the benzyl ketones. The catalyst rather than the solvent appeared to be the proton source since *p*-dimethylaminobenzylideneacetone was reduced at palladised charcoal in ethyl acetate to the same mixed product (*i.e.*, VIII, IX) as was obtained in alcohol. The hydrogenation of benzylideneacetone was accelerated by addition of acid. These observations are most simply related to carbonyl reduction *via* the conjugate acid (VII), formed at the catalyst surface. This view was supported by quantitative reduction of *p*-hydroxybenzylideneacetone and piperonylideneacetone at palladium on strontium carbonate to the benzyl ketones.

$$\underset{\text{(VIII)}}{ArCH_2{\cdot}CH_2{\cdot}COMe} \longleftarrow ArCH{:}CH{\cdot}COMe \xrightarrow{H^+} \underset{\text{(VII)}}{ArCH{:}CH{\cdot}CMe{:}\overset{+}{O}H} \longrightarrow \underset{\text{(IX)}}{ArCH_2{\cdot}CH_2{\cdot}CHMe{\cdot}OH}$$

The product of absorption of 1 mole of hydrogen by (+)-β-cyperone (X) in alkaline ethanol was found by ultraviolet analysis to be ~20% recovered β-cyperone, 60% of a conjugated ketone ($\lambda_{max.}$ 249 mμ), and 20% of the tetrahydro-derivative. This composition is similar to that of the reduction of β-cyperone at a lead-poisoned catalyst in benzene,[15] and on this basis the conjugated ketone is clearly (XI). Woodward and his co-workers [16] refer to the importance of an aprotic medium for partial (4,5) hydrogenation of a dienone; use of alkali may sometimes offer a useful alternative.

β-Ionone was reduced in alkali to the expected mixture of conjugated and unconjugated dihydro-ionones, after absorption of one mole of hydrogen.[17] In α-ionone the olefinic bond is known to be the less readily hydrogenated; [18] the presence of alkali increased this contrast.

Alkaline conditions sometimes favour reduction to the *cis*- rather than to the *trans*-decalone of compounds of general type (XIII) in the steroid [7,19] and sesquiterpene field.[1] The octalones (XII) and (XIII) were examined since the ethoxycarbonyl derivative (XIII) yields [20] exclusively the *trans*-, and the methyl analogue (XII) mainly the *cis*-decalone [21] on hydrogenation in alcohol. We obtained the same products and at closely the same rate in alcohol and in alkali.



(X) (XI) (XII) (XIII) (XIV)

The conformation (XIV) shows a molecule predisposed to absorption on the upper face, *i.e.*, to reduction to the *cis*-decalone provided the group R is not too large, *e.g.*, Me, with reduction to the *trans*-decalone as a more difficult, competing process which becomes important when the group R, *e.g.*, CO_2Et, offers serious hindrance to absorption. The behaviour of examples (XII) and (XIII) shows that alkali does not here alter fundamentally the mode of absorption or the process of hydrogen transfer.

Although a minor proportion of *trans*-olefin is frequently formed, semi-hydrogenation of acetylenes is the most convenient route to *cis*-olefins. On reduction at palladium,[22]

[15] Howe and McQuillin, *J.*, 1956, 2670.
[16] Woodward, Sondheimer, Taub, Heusler, and MacLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.
[17] Naves and Aridizio, *Helv. Chim. Acta*, 1949, **32**, 206.
[18] Naves, *ibid.*, 1947, **30**, 769.
[19] Cf. Slomp, Shealy, Johnson, Donia, Johnson, Holysz, Pederson, Jensen, and Ott, *J. Amer. Chem. Soc.*, 1955, **77**, 1216, and for earlier references.
[20] Dauben, Tweit, and MacLean, *ibid.*, p. 48.
[21] Dauben, Rogan, and Blanz, *ibid.*, 1954, **76**, 6384; du Feu, McQuillin, and Robinson, *J.*, 1937, 53; Linstead, Millidge, and Walpole, *J.*, 1937, 1140.
[22] Johnson, *J.*, 1946, 1014; Raphael, *J.*, 1952, 401.

and in most instances at Raney nickel,[23] butyne-1,4-diol gives *cis*-but-2-ene-1,4-diol. We obtained *cis*-but-2-ene-1,4-diol in alcohol, but in presence of alkali, the product contained a high proportion of the *trans*-isomer. *cis*-But-2-ene-1,4-diol was not inverted in alcoholic alkali with palladised charcoal in nitrogen. The *trans*-isomer is therefore a primary reduction product. Salkind[24] found the corresponding *cis*- and *trans*-1,4-dimethylhex-2-ene-1,4-diols similarly resistant to inversion by contact with catalyst in alcohol.

Hydrogen adds to acetylenedicarboxylic acid and its ester predominantly *trans* under some conditions.[25] From monopotassium acetylenedicarboxylate we obtained fumarate by reduction in water or aqueous alkali.

Hydrogen addition to acetylenes is generally predominantly *cis* at a zinc–copper couple,[26] but acetylenedicarboxylic [26] and phenylpropiolic acid [27] are again exceptional. The rôle of the carboxyl group in promoting inversion suggests an intermediate in reduction of butyne-1,4-diol which is of longer life in presence of alkali.

For the compounds in the Table, of which each group contains varied examples, sensitiveness to alkali retardation of hydrogenation is apparently associated with the chemical type of unsaturated centre present; in the earlier examples [1,2,7] the differential effect of alkali was observed for different centres in the same molecule. Such a correlation could be fortuitous; by being rapidly reduced, or very strongly absorbed, a substance could be especially sensitive to access of hydrogen to the catalyst with which alkali might physically interfere. The measured rates of hydrogen uptake (in absence of alkali) were, however, of the same order, with in each group an appreciable range, *viz.* (*a*) 0·06—5, (*b*) 1·3—6, (*c*) 0·1—10, and (*d*) 0·8—4 c.c./min. Acetylenes are very strongly absorbed, and commonly more strongly than the related olefin. The acetylenes appear, however, to be less sensitive to alkali retardation than the olefin. These reasons, the altered steric result of reduction of butyne-1,4-diol, and the instances of alkali catalysis suggested that the influence of alkali may be at the stage of hydrogen transfer.

The hydrogenation of guaiazulene was strongly inhibited by alkali but accelerated in alcohol by addition of a little, but not further by larger amounts of perchloric acid. This azulene was included as a basic type of hydrocarbon known to be reversibly protonated in acid solution. Protonation at the catalyst surface would therefore merit consideration as a step in olefin reduction.

Experimental

$[\alpha]_D$ and $\lambda_{max.}$ refer to solutions in chloroform and ethyl alcohol, respectively, and infrared data to liquid film (0·01 mm.) or potassium bromide disc as appropriate.

Method.—The compound was introduced in a glass bucket which could be dropped into the contents of the vessel after the catalyst had been saturated with hydrogen at atmospheric pressure. The less soluble compounds were dissolved in a small volume of the solvent being used. The catalyst, prepared after Linstead and Thomas [5] from palladous chloride (1·8 g.) and activated charcoal (2·2 g.) by reduction with alkaline formaldehyde, was washed with acetic acid and then with water to neutrality.

Results.—Details are given in parentheses following the name of the compound in the following order: amount of compound hydrogenated (g.), amount of catalyst used (g.), temperature, rate of uptake in 30 c.c. of alcohol (c.c./min.), rate of uptake in 30 c.c. of 2% alcoholic potassium hydroxide (c.c./min.).

Cholest-4-en-3-one (0·199, 0·04, 23°, 0·8, 0·73). The product, isolated in each case by chromatography, afforded coprostan-3-one, m. p. 62°, from ethanol.

(+)-*Carvone* (0·531, 0·106, 18°, 5·7, 4·9). The product from reduction in alcohol had b. p. 120°/14 mm., n_D^{20} 1·4881, $[\alpha]_D$ −2·76° (*c* 5·17), showed infrared bands at 1704 (>C=O) and 1661 cm.$^{-1}$ (>C=C–C–C=O), and was clearly a mixture. The material from reduction in alkali

[23] Marvel and Young, *J. Amer. Chem. Soc.*, 1951, **73**, 1066; Romanet, *Compt. rend.*, 1953, **236**, 1044, 1176; Valette, *Ann. Chim.*, 1948, **3**, 644.
[24] Salkind, *Ber.*, 1923, **56**, 187.
[25] Ott and Schroter, *Ber.*, 1927, **60**, 624.
[26] Clark and Crombie, *Chem. and Ind.*, 1957, 143.
[27] Barth and Glemser, *Ber.*, 1934, **67**, 1669.

XUM

had b. p. 120°/14 mm., and showed only saturated carbonyl absorption at 1709 cm.$^{-1}$, n_D^{20} 1·4701, $[\alpha]_D$ −13·5° (*c* 4·7), in agreement with (−)-dihydrocarvone [28] (n_D^{20} 1·4716, $[\alpha]_D$ −16° liquid); the 2,4-dinitrophenylhydrazone had m. p. and mixed m. p. 146°.

(+)-*Carvotanacetone* (0·533, 0·10, 20°, 3·9, 2·6). The product from reduction in alcohol had b. p. 90°/11 mm., n_D^{20} 1·4606, and showed infrared absorption at 3408 cm.$^{-1}$ (OH). The material from reduction in alkali had b. p. 90°/11 mm., n_D^{20} 1·4551, $[\alpha]_D$ −11·7° (*c* 5·3), values agreeing closely with those for (−)-tetrahydrocarvone [29] (n_D^{30} 1·4531, $[\alpha]_D^{30}$ −9·3°, liquid). The 2,4-dinitrophenylhydrazone had m. p. and mixed m. p. 150°.

Mesityl oxide (0·348, 0·07, 20°, 6·5, 4·3). The product, after completion of reduction, in each case gave isobutyl methyl ketone semicarbazone, m. p. 132—133° (Wieland [30] gives m. p. 130°).

2,3,4,5,6,7,8,10-*Octahydro*-10-*methyl*-2-*oxonaphthalene* (0·49 0·07, 17·5°, 2·1, 2·7). The products, b. p. 60°/0·1 mm., n_D^{20} 1·4918 and 1·4940, respectively gave the same infrared spectra and when seeded gave *cis*-10-methyl-2-decalone, m. p. 37° (cf. du Feu, McQuillin, and Robinson, and Dauben, Rogan, and Blanz [21]).

10-*Ethoxycarbonyl*-2,3,4,5,6,7,8,10-*octahydro*-2-*oxonaphthalene* (0·08, 0·015, 16°, 0·35, 0·35, 3 c.c. of solution being used in each case). 10-Ethoxycarbonyl-2-decalone isolated from both experiments gave identical infrared spectra and the semicarbazone, m. p. 194°, of the pure *trans*-ketone, from aqueous ethanol (Dauben, Tweit, and MacLean [20] give n_D^{25} 1·4790; semicarbazone, m. p. 193—194°).

α-*Ionone* (0·349, 0·05, 19°, 0·9, 1·7). The product from alkaline reduction showed only saturated carbonyl absorption (1715 cm.$^{-1}$), and at 3031 and 813 cm.$^{-1}$ bands corresponding to the group >C=CH−; the 2,4-dinitrophenylhydrazone had m. p. 101° (cf. Naves and Lecomte [31]).

7,11-*Dioxolanost*-8-*en*-3β-*ol* (0·165, 0·032, 19°). In dioxan–alcohol (3 : 1; 50 c.c.) there was negligible absorption of hydrogen (0·2 c.c. in 15 min.). After addition of 60% perchloric acid (4 drops) hydrogen was absorbed at 1·3 c.c./min. In dioxan–alcohol (3·1; 50 c.c.) containing potassium hydroxide (0·5%) the uptake was initially 0·17 c.c./min. A product, m. p. 186°, $[\alpha]_D$ +26·9° (*c* 5·21), was isolated directly from the alkaline reduction and from reduction in acid after chromatography. Dorée, McGhie, and Kurzer [9] give m. p. 184°, $[\alpha]_D$ +25·7° for 7,11-dioxolanostan-3β-ol.

7,11-*Dioxolanost*-8-*en*-3β-*yl acetate* (0·494, 0·051, 24°). (*a*) In dioxan–alcohol (3 : 1; 50 c.c.) hydrogen uptake was very slow (3·1 c.c. in 49 min.); after addition of acetic acid (1 c.c.) the initial rate was 0·7 c.c./min. (*b*) In dioxan–alcohol (3 : 1; 50 c.c.) with 60% perchloric acid (0·1 c.c.) the uptake was 0·6 c.c./min. (*c*) In dioxan–alcohol (3 : 1; 50 c.c.) containing potassium hydroxide (0·5%) the initial uptake was 0·25 c.c./min. The products from reduction in acid solution isolated by chromatography gave 7,11-dioxolanostan-3β-yl acetate, m. p. 224°, $[\alpha]_D$ +56·3° (*c* 4·8) (Dorée, McGhie, and Kurzer [9] give m. p. 222—224°, $[\alpha]_D$ +54·6°). Hydrolysis of the product of reduction in alkali gave 7,11-dioxolanostan-3β-ol, m. p. 186° (cf. Dorée, McGhie, and Kurzer [9]).

Sodium anthraquinone-2-*sulphonate* (0·285, 0·057, 21°). In water (50 c.c.) and in sodium hydroxide (2%; 50 c.c.), hydrogen uptake was 1·45 c.c./min.

Propargyl alcohol (0·09 g., 0·019, 17°). In alcohol hydrogen uptake for the first step was 1·5 c.c./min. and for the second 7 c.c./min.; in alkali for the first step 0·5, and for the second 1·8 c.c./min.

Butyne-1,4-*diol* (0·147, 0·03, 18°, 4·0 + 3·0, 0·8 + 0·5). The product, b. p. 130°/20 mm., n_D^{20} 1·4710, of semireduction of butyne-1,4-diol (0·29 g.) in alcohol gave *cis*-but-2-ene-1,4-diol dibenzoate, m. p. 67°, in 91% yield (Clarke and Crombie [30] give m. p. 67°).

cis-But-2-en-1,4-diol (0·29 g.), prepared in this way, was shaken in alcoholic sodium hydroxide (2%, 50 c.c.) with palladised charcoal (0·32 g.) in nitrogen for some hours; it gave the same dibenzoate, m. p. 67°, in excellent yield.

The product of semireduction of butyne-1,4-diol (1·5 g.) in alcoholic sodium hydroxide (0·1%; 40 c.c.) had b. p. 127°/20 mm., n_D 1·4680. Its dibenzoate, m. p. 101° [from petroleum (b. p. 100—120°) and then methanol], was formed in substantial yield. For *trans*-but-2-ene-1,4-diol dibenzoate Prévost and Lutz [32] give m. p. 101°.

[28] Semmler and Feldstein, *Ber.*, 1914, **47**, 384.
[29] Simonsen and Rau, *J.*, 1922, 876.
[30] Wieland, *Ber.*, 1925, **58**, 2016.
[31] Naves and Lecomte, *Bull. Soc. chim. France*, 1953, 112.
[32] Prévost and Lutz, *Compt. rend.*, 1934, **198**, 2264.

Complete hydrogenation in alcohol gave butane-1,4-diol (dibenzoate, m. p. 81° cf. Hamonet [33])].

Pent-2-yne-1,4-diol (0·178, 0·035, 20°, 6 + 7·5, 1·4 + 1·1).

1-Ethynylcyclohexan-1-ol (0·221, 0·043, 18°, 6·5 + 10, 6·5 + 1·6).

The products, b. p. 63°/13 mm., n_D^{20} 1·4618, from alcohol reduction, and n_D^{20} 1·4620, from reduction in alkali (Found: C, 74·8; H, 12·6; and C, 75·0; H, 12·5; respectively. Calc. for $C_8H_{14}O$: C, 75·0; H, 12·5%) gave the same infrared spectra. Wallach [34] gives n_D^{20} 1·4638 for 1-ethylcyclohexan-1-ol.

Phenylacetylene (0·182, 0·038, 19°, 4·0 + 5·6, 2·6 + 3·7).

Potassium acetylenedicarboxylate (0·369, 0·074 g, 19·5°, 2·5, 1·05). The product from both experiments, isolated and recrystallised from water, was fumaric acid, sublimed ~200°, identical with an authentic specimen.

(−)-*Dihydrocarvone* (0·536, 0·096, 17°, 3·2, 0·42). The products, b. p. 125°/14 mm., n_D^{20} 1·4579, $[\alpha]_D$ −11·3° (*c* 5·18), from reduction in alcohol, and n_D^{20} 1·4579, $[\alpha]_D$ −13·3° (*c* 5·03), from alkali both gave a 2,4-dinitrophenylhydrazone, m. p. 149°, in agreement with that of (−)-tetrahydrocarvone.[29]

Hexa-2,4-dien-1-ol (0·173, 0·034, 24°, 10·1, 1·8). After absorption of 2 mols. of hydrogen in alcohol hexan-1-ol, b. p. 90°/34 mm., n_D^{20} 1·3964, was isolated (Behal [35] gives n_D^{20} 1·4133). After absorption of 1 mol. of hydrogen in alkaline alcohol hexenol was isolated, b. p. 95°/32 mm., n_D^{20} 1·4280; it showed strong bands at 972 and 1698 cm.$^{-1}$ (*trans*-CH=CH–).

Guaiazulene (0·101, 0·025, 19°).

Initial rates of reduction (*a*) in alcohol (30 c.c.), and in the same solvent containing (*b*) 0·1 c.c. and (*c*) 1·0 c.c. of 60% perchloric acid were 0·1, 0·27, and 0·28 c.c./min. respectively.

In alcoholic potassium hydroxide (0·1%, 30 c.c.) there was no uptake of hydrogen. Complete reduction in alcohol took 50 c.c. of hydrogen (theory for 4 double bonds, 49 c.c.).

Benzylideneacetone (0·141, 0·029, 19°). Hydrogen uptake in (*a*) alcohol (40 c.c.), (*b*) alcoholic potassium hydroxide (2%, 40 c.c.), and (*c*) alcohol (40 c.c.) with hydrochloric acid (2 drops) was 1·6, 0·8, and 2·9 c.c./min.

The products isolated from experiments (*a*) and (*b*) had b. p. 110—115°/12 mm., n_D^{20} 1·5095 and n_D^{20} 1·5090 respectively, and gave a semicarbazone, m. p. 142° (Klages [36] gives m. p. 142° for the semicarbazone of benzylacetone).

p-*Dimethylaminobenzylideneacetone* (0·141, 0·03, 19°). Hydrogen uptake in (*a*) alcohol (40 c.c.), (*b*) alcoholic potassium hydroxide (2%; 40 c.c.), and (*c*) ethyl acetate (40 c.c.) was 1·3, 0·35, and 0·55 c.c./min.

The product from experiment (*b*) was *p*-dimethylaminobenzylacetone, b. p. 70°/0·1 mm., m. p. 49° (from aqueous alcohol) (Rupe, Collin, and Schmiderer [37] give m. p. 50·5°). The products from (*a*) and (*c*), respectively n_D^{20} 1·5450 and 1·5439, failed to crystallise. The infrared spectra showed bands at 3425 cm.$^{-1}$ (OH, strong), 1712 and 1621 cm.$^{-1}$ (>CO and Ar·C=C·CO), and 947 cm.$^{-1}$ (·CH=CH·).

p-*Chlorobenzylideneacetone* (0·136, 0·029, 21°, 2·2, 0·7; 40 c.c. were used in each experiment). The product of reduction in alcohol had b. p. 110°/0·3 mm., n_D^{20} 1·5502 and showed strong infrared absorption at 3474 (OH), 1605 (ArCH=CH·CO), and 978 cm.$^{-1}$ (·CH=CH·). The product from reduction in alkali had n_D^{20} 1·5250 and showed strong carbonyl absorption at 1715 cm.$^{-1}$. It was clearly *p*-chlorobenzylacetone, giving a *semicarbazone*, m. p. 153—154° (from ethanol) which was phototropic (Found: C, 54·6; H, 6·0. $C_{11}H_{14}ON_3Cl$ requires C, 55·0; H, 5·8%).

p-*Methoxybenzylideneacetone* (0·132, 0·027, 20°, 2·4, 0·48; 40 c.c. were used in each experiment). The product, b. p. 105°/0·3 mm., n_D^{20} 1·5462, from reduction in alcohol showed strong absorption at 3435 (OH) and 1607 cm.$^{-1}$ (ArCH=CH·CO·). The product, n_D^{20} 1·5179, from alkali showed strong carbonyl absorption at 1712 cm.$^{-1}$ and was characterised as the semicarbazone, m. p. 169° (from alcohol). Strauss and Grindel [38] give m. p. 169—170° for *p*-methoxybenzylacetone semicarbazone.

3,4-*Methylenedioxybenzylideneacetone* (0·1, 0·021, 18°, 1·2, 0·16; 40 c.c. were used in each

[33] Hamonet, *Bull. Soc. chim. France*, 1905, **33**, 523.
[34] Wallach, *Annalen*, 1908, **360**, 26.
[35] Behal, *Bull. Soc. chim. France*, 1919, **25**, 473.
[36] Klages, *Ber.*, 1904, **37**, 2301.
[37] Rupe, Collin, and Schmiderer, *Helv. Chim. Acta*, 1931, **14**, 1340.
[38] Straus and Grindel, *Annalen*, 1924, **439**, 276.

XUM

experiment). From reduction in alkali 3,4-methylenedioxybenzylacetone was isolated, m. p. 50°; it was also obtained with some difficulty from reduction in alcohol. It was more conveniently obtained by reduction in ethyl acetate using a palladised strontium carbonate catalyst; it then had m. p. 51° without purification (Vavon and Faillebin [39] give m. p. 50—51° for 3,4-methylenedioxybenzylacetone).

p-*Hydroxybenzylideneacetone* (0·122, 0·025, 18°, 0·8, 0·17; 40 c.c. were used in each experiment). *p*-Hydroxybenzylacetone, m. p. 82—83°, was obtained in each case; reduction in alkali gave much the purer product. The use of palladised strontium carbonate and ethyl acetate gave a pure product directly. For *p*-hydroxybenzylacetone Mannich and Merz [40] give m. p. 83—84°.

(+)-β-*Cyperone* (0·22, 0·035, 17·5°, 1·6, 0·35). The product from absorption of 1 equivalent of hydrogen in alkali had n_D^{20} 1·5164, $\lambda_{max.}$ 249 and 298 mμ (ε 9499 and 5129).

β-*Ionone* (0·354, 0·05, 22°, 3·2, 0·6). Hydrogenation was complete in alcohol to give a tetrahydroionone, b. p. 90°/0·2 mm., n_D^{20} 1·4695. In alkaline solution reduction was only a little over half complete; the product had n_D^{20} 1·4808, $\lambda_{max.}$ 229 mμ, ε 6022.

The authors thank Professor John Read, F.R.S., Dr. J. F. McGhie, and Dr. T. G. Halsall for gifts of chemicals, and the Department of Scientific and Industrial Research for an award (to W. O. O.).

KING'S COLLEGE, NEWCASTLE UPON TYNE. [*Received*, 29*th August*, 1958.]

[39] Vavon and Faillebin, *Compt. rend.*, 1919, **169**, 65.
[40] Mannich and Merz, *Arch. Pharm.*, 1927, **265**, 22.

---

582. B-*Nor*-5α-*cholestane*, B-*Nor*-5β-*cholestane*, *and Related Compounds*.

By G. H. R. SUMMERS.

Partial syntheses of B-nor-5α- and B-nor-5β-cholestane are described.

DURING an investigation of the stereochemistry of some B-nor-6-oxo-steroids we obtained results which required the preparation of the reference compounds B-nor-5α- and B-nor-5β-cholestane. In the literature two hydrocarbons have been reported as possessing the B-norcholestane structure, but the stereochemistry of only one of them has been examined and that not conclusively. We now describe the preparation of authentic B-nor-5α- and B-nor-5β-cholestane and thus clarify a situation which was previously confused.

Hydrogenation of either B-norcholest-5-ene or B-norcholesta-3 : 5-diene with platinum in acetic acid [1] rapidly yielded a hydrocarbon, m. p. 45°. With platinum in ether it was slow and the product a mixture from which an isomeric hydrocarbon, m. p. 80°, was isolated. No further information about the latter compound is available, but the former has been assigned both the A/B-*cis*- and the A/B-*trans*-configuration by independent workers: Fieser,[2] who prepared the hydrocarbon, m. p. 45°, $[\alpha]_D$ +10°, by reduction of Butenandt and Hausmann's diketone [3] (considered to be B-nor-5β-cholestane-3 : 6-dione) by the Wolff–Kishner method and *via* the bisethylene thioketal, gave it the *cis*-perhydroindane structure. This decision was supported by the fact that the diketone failed to isomerise at position 5 under acid or alkaline conditions, and by the relation, then generally accepted, that *cis*-perhydroindanes were more stable than their *trans*-isomers.[4] Dauben and Fonken,[5] however, favoured the alternative *trans*-structure for the low-melting hydrocarbon and prepared it by another route. Hydrogenation of B-norcholest-5-en-3β-ol (B-norcholesterol [6]) with platinum in acetic acid gave B-nor-5α-cholestan-3β-ol, oxidised to

[1] Windaus, *Ber.*, 1920, **53**, 488; cf. Lettré, *Z. physiol. Chem.*, 1933, **218**, 67.
[2] Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4386.
[3] Butenandt and Hausmann, *Ber.*, 1937, **70**, 1154.
[4] Drieding, *Chem. and Ind.*, 1954, 992.
[5] Dauben and Fonken, *J. Amer. Chem. Soc.*, 1956, **78**, 4736.
[6] Šorm and Dykova, *Coll. Czech. Chem. Comm.*, 1948, **13**, 407.

B-nor-5α-cholestan-3-one and thence reduced by the Wolff–Kishner method to B-nor-5α-cholestane, m. p. 45—46°, $[\alpha]_D$ +11°. Their reversal of Fieser's original assignment was based on the assumption that the conformations of B-nor-5α-cholestane and 5α-cholestane were substantially identical as demonstrated by the chemical and spectral properties of the above intermediates and particularly B-nor-5α-cholestan-3β-ol. Our suspicions that Dauben and Fonken's B-nor-5α-cholestan-3-one was an A/B-*cis*-compound were confirmed by the measurement by Djerassi, Marshall, and Nakano [7] of its optical rotatory dispersion. This present work supports this observation and places on a firmer basis the stereochemistry at position 5 of the B-nor-compounds described above.

Catalytic hydrogenation of 3β-acetoxy-B-norcholest-5-ene (I; R = Ac) with platinum–acetic acid occurred rapidly to give, after hydrolysis, a mixture of two alcohols, double m. p. 58—60° and 76—77°, $[\alpha]_D$ +16° (81%), and m. p. 132°, $[\alpha]_D$ −9° (16%), which from their relative ease of elution from alumina were considered to be B-nor-5β- (II; R = H) and B-nor-5α-cholestan-3β-ol (V; R = H) respectively. (Dauben and Fonken [5] record m. p. 77—78° and $[\alpha]_D$ −30·8° for B-nor-5α-cholestan-3β-ol, and m. p. 62—64° and $[\alpha]$ −9·8° for B-nor-5α-cholestan-3-one although the specific rotations calculated from their own molecular-rotation data are respectively +16° and +19°.) A similar result was obtained with platinum–ethyl acetate–perchloric acid, but in ethyl acetate alone no hydrogenation occurred. Addition of a little acetic acid as promoter caused slow uptake of hydrogen and the yield of alcohol (V) was increased to 47%. These results recall the influence of solvent on the stereochemical course of reduction of Δ^4- and Δ^5-steroids,[8,9] and bear comparison with the results of hydrogenation of A-norcholest-3-enes [10,11] and Δ^{14}-steroids.[12] In acid solution 3-methyl-A-norcholest-3-ene and its unmethylated homologue give mixtures, whereas normal reduction of a 14 : 15-double linkage yields C/D-*trans*-steroids although the epimeric C/D-*cis*-compound can be formed when α-orientated bulky neighbouring groups are present at, *e.g.*, position 17 (ref. 13) or even 11 (ref. 14).

Oxidation of the alcohol (II; R = H) with chromium trioxide in pyridine gave B-nor-5β-cholestan-3-one (III), the structure of which was confirmed by reduction to B-nor-5β-cholestan-3α-ol (VII; R = H) in quantitative yield by lithium aluminium hydride. The production of the 3α-alcohol is contrary to Dauben and Fonken's result,[5] but consistent with the reduction of 3-oxo-A/B-*cis*-steroids by metal hydrides.[15] With " unhindered " ketones of this type where approach of the aluminium hydride ion can occur with equal facility from either face of the molecule, the product is determined by the relative stability of the two possible intermediate transition states and thus reduction of a 3-oxo-A/B-*cis*-steroid yields predominantly the equatorial 3α-alcohol.

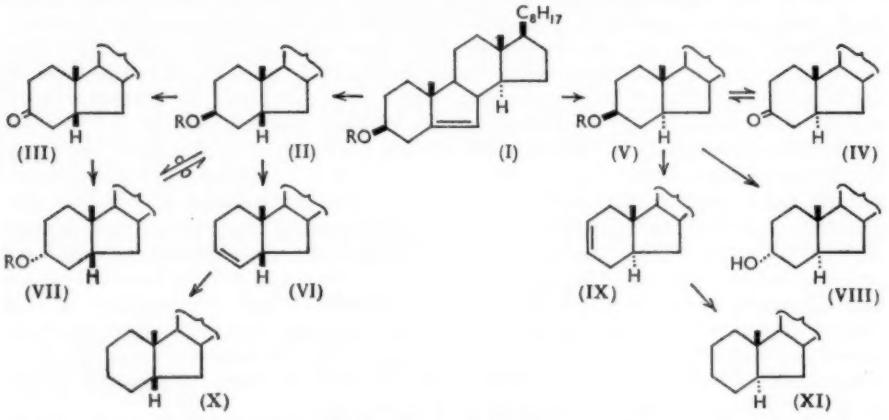
The 3α-alcohol (VII; R = H) was also obtained by acetolysis of B-nor-5β-cholestan-3β-yl toluene-*p*-sulphonate (II; R = $C_6H_4Me{\cdot}SO_2$), followed by hydrolysis and chromatography of the product. In this solvolysis the alcohol (VII; R = H) was accompanied by an oily hydrocarbon which we consider to be B-nor-5β-cholest-3-ene (VI) by analogy with the behaviour shown by 5β-cholestan-3α-yl and -3β-yl toluene-*p*-sulphonate under identical conditions.[16] Replacement reactions of saturated steroid 3α- and 3β-yl toluene-*p*-sulphonates on aluminium oxide [17] reproduce qualitatively the results (inversion and

[7] Djerassi, Marshall, and Nakano, *J. Amer. Chem. Soc.*, 1958, **80**, 4853.
[8] Agashe, Shoppee, and Summers, *J.*, 1957, 3107.
[9] Lewis and Shoppee, *J.*, 1955, 1365.
[10] Lettré, *Z. physiol. Chem.*, 1933, **221**, 73.
[11] Schmid and Kagi, *Helv. Chim. Acta*, 1950, **33**, 1581; Shoppee and Summers, *J.*, 1952, 2528.
[12] For many references see Lettré, Inhoffen, and Tschesche, " Sterine, Gallensauren und verwandte Naturstoffe," Enke, Stuttgart, 1954, Vol. I, p. 287 *et seq.*
[13] Speiser and Reichstein, *Helv. Chim. Acta*, 1947, **30**, 2143; 1948, **31**, 623.
[14] Meyer, *ibid.*, 1949, **32**, 1599.
[15] Shoppee and Summers, *J.*, 1950, 687; Dauben, Fonken, and Knoyle, *J. Amer. Chem. Soc.*, 1956, **78**, 2579; Dauben, Blanz, Jiu, and Micheli, *ibid.*, p. 3752; Wheeler and Mateos, *Canad. J. Chem.*, 1958, **36**, 1431; see also criticisms by Hardy and Wicker, *J. Amer. Chem. Soc.*, 1958, **80**, 640.
[16] Shoppee, *J.*, 1946, 1138; Bridgewater and Shoppee, *J.*, 1953, 1709.
[17] Chang and Blickerstaff, *Chem. and Ind.*, 1958, 590.

XUM

elimination) of bimolecular hydrolysis in solution,[16] and we find that chromatography of the toluene-*p*-sulphonate (VII; R = $C_6H_4Me{\cdot}SO_2$) on basic alumina gives B-nor-5β-cholest-3-ene (VI) and the 3β-alcohol (II; R = H). The parent hydrocarbon B-nor-5β-cholestane (X) was obtained by (*a*) reduction of the toluene-*p*-sulphonates (II and VII; R = $C_6H_4Me{\cdot}SO_2$) with lithium aluminium hydride and (*b*) catalytic hydrogenation of B-nor-5β-cholest-3-ene (VI).

The same reactions applied to B-nor-5α-cholestan-3β-ol (V; R = H), and similarly interpreted, support the correctness of its formulation as an A/B-*trans*-compound. Oxidation with chromium trioxide in pyridine gave B-nor-5α-cholestan-3-one (IV) which by



reduction with lithium aluminium hydride or sodium in propanol regenerated the 3β-alcohol (V; R = H) in accord with a 3-oxo-A/B-*trans*-structure for the ketone (IV).[15] The epimeric 3α-alcohol (VIII) was prepared for comparison by chromatography of B-nor-5α-cholestan-3β-yl toluene-*p*-sulphonate (V; R = $C_6H_4Me{\cdot}SO_2$) on basic alumina. Reduction of this ester with lithium aluminium hydride yielded B-nor-5α-cholestane (XI), also prepared by hydrogenation of a hydrocarbon assumed by analogy * with the similar behaviour of 5α-cholestan-3β-yl toluene-*p*-sulphonate to be B-nor-5α-cholest-2-ene (XI), which was the principal product of the chromatographic decomposition of the ester (V; R = $C_6H_4Me{\cdot}SO_2$).

Our stereochemical assignments are supported by the optical rotatory dispersion curves of the ketones (III and IV). The asymmetric environment of a carbonyl group in a cyclic system is reflected in its rotatory dispersion curve which thus detects conformational changes. The ketones (III and IV) in methanol gave single Cotton-effect curves [19] respectively negative and positive (amplitudes expressed as molecular rotations, −6000° and +7300°). These values may be compared with values of −2700° and 6500° for 5β- and 5α-cholestan-3-one respectively,[20] and on the basis of simple analogy the data support the allotment of the configurations given here to the B-nor-ketones [cf. Djerassi, Marshall, and Nakano,[7] who measured the 5β-B-nor-compound only; our values for (III) agree closely with theirs]. Consideration of the rotation data in the light of the " octant rule " confirms this allotment.[21]

* Hydrocarbon (IX) could possibly be B-nor-5α-cholest-3-ene since it seems that extra strain in ring B can influence the relative reactivities of positions 2 and 4, *e.g.*, methylation of 5α-cholest-7-en-3-one gives the 4α-methyl and not the expected 2α-methyl compound.

[18] Wells and Neiderhiser, *J. Amer. Chem. Soc.*, 1957, **79**, 6569; Mazur and Sondheimer, *ibid.*, 1958, **80**, 6296.

[19] For nomenclature see Djerassi and Klyne, *Proc. Chem. Soc.*, 1957, 55.

[20] Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362.

[21] Personal communication from Dr. W. Klyne.

Dauben and Fonken [5] consider that the infrared spectra of their alcohol and its acetate further support its formulation as B-nor-5α-cholestan-3β-ol. Since the alcohol displayed bands at 1040 and 1076 cm.$^{-1}$, and the acetate a single strong band at 1242 cm.$^{-1}$, they concluded by analogy that these were consistent with the presence of an equatorial hydroxyl group and an A/B-*trans* ring junction. The Table gives the frequencies of the principal absorption bands found in the range 990—1050 cm.$^{-1}$ for the epimeric pairs of cholestan-3-ols and B-norcholestan-3-ols. The latter also gave bands of low intensity in the 1070—1090 cm.$^{-1}$ region.

Frequencies (cm.$^{-1}$) of the intense bands in the range 990—1050 cm.$^{-1}$ (in carbon disulphide) for 3α- and 3β-hydroxycholestanes and β-norcholestanes.

Equatorial		*Axial*	
5α-Cholestan-3β-ol	1038	5α-Cholestan-3α-ol	1002
B-Nor-5α-cholestan-3β-ol	1048, 1009	B-Nor-5α-cholestan-3α-ol	1048, 1009, 998
5β-Cholestan-3α-ol	1038	5β-Cholestan-3β-ol	1034
B-Nor-5β-cholestan-3α-ol	1047	B-Nor-5β-cholestan-3β-ol	1042

In saturated steroids an equatorial 3-hydroxyl group gives a strong band due to the C–O stretching vibration near 1040 cm.$^{-1}$: an axial group absorbs at a lower frequency usually in the range 1000—1040 cm.$^{-1}$.[22] The absorption bands for the B-nor-5β-cholestan-3-ols conform to this pattern, the higher frequency being probably attributable to distortion of ring A by fusion with a cyclopentane ring. The spectra for the B-nor-5α-cholestan-3-ols are more complex owing to the presence of additional more intense bands about 1000 cm.$^{-1}$ which on the basis of simple analogy are difficult to interpret with certainty. Thus although conclusions as to the stereochemistry on the basis of analogy with spectral details of the cholestan-3-ols can be drawn, we feel that until further information about perhydroindanols of this type becomes available interpretation must be made with caution.

This work supports the original findings of Fieser [2] and leads to the conclusion that the most stable conformation of B-nor-steroids features an A/B-*cis*-ring fusion. Thus reduction of B-norcholest-4-en-3-one by lithium–ammonia,[5] a reagent which usually yields the thermodynamically more stable product,[23] gives B-nor-5β-cholestan-3-one (III). Also zinc–acetic acid reduction of B-norcholest-4-ene-3,6-dione [2,5] and 3-oxo-6,7-secocholest-4-ene-6,7-dioic acid [2] afford the 5β-isomers. It has recently been reported that catalytic reduction of 3β-hydroxy-B-norandrost-5-en-17-one yields 3β-hydroxy-B-nor-5α-androstan-17-one;[24] we feel this hydrogenation should be reconsidered in the light of the above experiments.

We wish to defer at present a detailed analysis of the conformations of these perhydroindanes and the related C-nor-D-homosteroids until information about the B/C-ring union becomes available.

Experimental

Infrared spectra were recorded on a Grubb–Parsons GS2 double-beam grating spectrometer. $[\alpha]_D$ are in chloroform.

B-*Nor*-5β- *and* B-*Nor*-5α-*cholestan*-3β-*ol*.—(*a*) 3β-Acetoxy-B-norcholest-5-ene {m. p. 79°, $[\alpha]_D$ −84° (*c* 1·1); 1·14 g.} was hydrogenated with platinum oxide (184 mg.) in acetic acid (80 ml.); the oily product was hydrolysed with 5% ethanolic potassium hydroxide (50 ml.) for 1 hr. and the resulting oil chromatographed on aluminium oxide (40 g.). Elution with ether (6 × 100 ml.) gave an oil (827 mg.) which on crystallisation from methanol gave B-*nor*-5β-*cholestan*-3β-*ol*, double m. p. 56—60° and 74—76°, $[\alpha]_D$ +17° (*c* 1·6) (Found: C, 83·5; H, 12·4. $C_{26}H_{46}O$ requires C, 83·35; H, 12·4%). Further elution with ether (4 × 100 ml.) gave B-*nor*-5α-*cholestan*-3β-*ol* (162 mg.), m. p. 132° (needles from acetone), $[\alpha]_D$ −9° (*c* 1·7) (Found: C, 83·1; H, 12·5%).

[22] Jones and Roberts, *J. Amer. Chem. Soc.*, 1958, **80**, 6121 and references there cited.
[23] Barton and Robinson, *J.*, 1954, 3045; Birch and Smith, *Quart. Reviews*, 1958, **12**, 17,
[24] Joska and Šorm, *Coll. Czech. Chem. Comm.*, 1958, **23**, 1377; Joska, Fajkos, and Šorm, *Chem. and Ind.*, 1958, 1665.

XUM

(*b*) 3β-Acetoxy-B-norcholest-5-ene (2·3 g.) in ethyl acetate (40 ml.) containing 60% perchloric acid (6 drops) was shaken with platinum oxide (200 mg.) in hydrogen until absorption ceased (20 min.). Working up as above followed by chromatography on aluminium oxide (100 g.) gave B-nor-5β-cholestan-3β-ol (1·95 g.), double m. p. 58—60° and 76—77°, [α] +16° (*c* 1·1), and B-nor-5α-cholestan-3β-ol (318 mg.), m. p. 131—132°.

(*c*) B-Nor-cholest-5-en-3β-ol {m. p. 116°, $[\alpha]_D$ −90° (*c* 1·0); 2·1 g.} in ethyl acetate (50 ml.) shaken with platinum oxide (200 mg.) failed to take up hydrogen. Absorption of hydrogen occurred slowly after the addition of acetic acid (12 drops) and was complete after 12 hr. Chromatography of the product gave B-nor-5β-, double m. p. 56—60° and 74° (1·03 g.), and -5α-cholestan-3β-ol, m. p. 129—131° (989 mg.).

B-*Nor*-5β-*cholestan*-3β-*yl Toluene*-p-*sulphonate*.—B-Nor-5β-cholestan-3β-ol (1·5 g.) in pyridine (15 ml.) was treated with toluene-*p*-sulphonyl chloride (1·5 g.) and left overnight. After the usual working up the *toluene*-p-*sulphonate* crystallised from ether as needles, m. p. 110—112°, $[\alpha]_D$ +10° (*c* 1·5) (Found: C, 75·2; H, 9·5. $C_{33}H_{52}O_3S$ requires C, 75·0; H, 9·9%).

B-*Nor*-5β-*cholestane*.—(*a*) The above toluene-*p*-sulphonyl ester (400 mg.) in ether (100 ml.) was heated under reflux with lithium aluminium hydride for 24 hr. The product, an oil, was chromatographed on aluminium oxide (15 g.). Elution with pentane (2 × 40 ml.) gave B-nor-5β-cholestane (259 mg.), m. p. 42—45°, $[\alpha]_D$ +8° (*c* 1·5) (from acetone), and elution with chloroform gave B-nor-5β-cholestan-3β-ol, m. p. 75—76° (49 mg.).

(*b*) B-Nor-5β-cholest-3-ene (157 mg.) in ethyl acetate containing 60% perchloric acid (4 drops) was hydrogenated in the presence of platinum oxide (50 mg.). The oily product crystallised from acetic acid to give B-nor-5β-cholestane, m. p. 45°, $[\alpha]_D$ +10° (*c* 1·0).

B-*Nor*-5β-*cholestan*-3-*one*.—B-Nor-5β-cholestan-3β-ol (1 g.) in pyridine (10 ml.) was treated with chromium trioxide (1 g.) in pyridine (10 ml.) and left overnight. After dilution with pentane the solution was filtered, and the filtrate evaporated in a vacuum. The oily product was chromatographed on aluminium oxide (30 g.). Elution with benzene–pentane (1 : 9; 6 × 100 ml.) gave B-*nor*-5β-*cholestan*-3-*one* (539 mg.), m. p. 68—70°, $[\alpha]_D$ +18·5° (*c* 1·2), $\nu_{max.}$ 1715 cm.$^{-1}$ in carbon tetrachloride (Found: C, 83·7; H, 11·75. $C_{26}H_{44}O$ requires C, 83·8; H, 11·9%). Elution with ether gave starting material (403 mg.). Rotatory dispersion in methanol (*c* = 0·1): [*M*] = −40 at 600 mμ; −1830 at 310 mμ (trough); +4080 at 265 mμ.

B-*Nor*-5β-*cholestan*-3α-*ol*.—(*a*) B-Nor-5β-cholestan-3-one (300 mg.) in ether (20 ml.) was left for 2 hr. at room temperature with lithium aluminium hydride (300 mg.). The oily product was chromatographed on aluminium oxide (20 g.). Elution with ether–benzene (1 : 1; 11 × 25 ml.) gave an oil (287 mg.) which crystallised. Crystallisation from a solvent was difficult and B-*nor*-5β-*cholestan*-3α-*ol* was obtained as an amorphous material, m. p. 89—92° (from ethyl acetate), $[\alpha]_D$ +9·5° (*c* 1·7) (Found: C, 83·2; H, 12·3. $C_{26}H_{46}O$ requires C, 83·35; H, 12·4%). The *toluene*-p-*sulphonate*, prepared in the usual way, crystallised from pentane as needles, m. p. 96—100°, $[\alpha]_D$ +17° (*c* 1·6) (Found: C, 74·6; H, 9·9. $C_{33}H_{52}O_3S$ requires C, 74·96; H, 10·0%).

(*b*) B-Nor-5β-cholestan-3β-yl toluene-*p*-sulphonate (879 mg.) in acetic acid (25 ml.) containing anhydrous potassium acetate (6 g.) was heated at 95° for 2·5 hr. The oily product was treated with lithium aluminium hydride in ether for 0·5 hr. The product was chromatographed on basic aluminium oxide (Woelm; 30 g.). Elution with pentane (2 × 100 ml.) gave B-nor-5β-cholest-3-ene (404 mg.) as an oil, $[\alpha]_D$ +20° (*c* 2·2); and elution with chloroform gave B-nor-3β-cholestan-3α-ol (214 mg.) which separated from ethyl acetate as hair-like crystals, m. p. 86—88°, $[\alpha]_D$ +12° (*ca.* 2·0). The infrared spectra of the two specimens were identical.

B-*Nor*-5β-*cholestan*-3β-*ol*.—B-Nor-5β-cholestan-3α-yl toluene-*p*-sulphonate (810 mg.) in benzene was adsorbed on basic alumina (Woelm) and left 4 days. Elution with pentane gave B-*nor*-5β-*cholest*-3-*one* (266 mg.) as an oil which crystallised with difficulty from acetone and then had m. p. 28—30°, $[\alpha]_D$ +7° (*c* 2·7) (Found: C, 87·3; H, 12·4. $C_{26}H_{44}$ requires C, 87·6; H, 12·4%). Elution with chloroform gave B-nor-5β-cholestan-3β-ol (247 mg.), m. p. and mixed m. p. 74—77°.

B-*Nor*-5α-*cholestan*-3β-*yl Toluene*-p-*sulphonate*.—B-Nor-5α-cholestan-3β-ol (700 mg.) in pyridine (10 ml.) was treated with toluene-*p*-sulphonyl chloride (650 mg.) and left for 2 days. The *toluene*-p-*sulphonate* crystallised from ether as needles, m. p. 123—125°, $[\alpha]_D$ −22° (*c* 2·0) (Found: C, 75·2; H, 9·6. $C_{33}H_{52}O_3S$ requires C, 74·96; H, 9·9%).

B-*Nor*-5α-*cholestane*.—(*a*) The last toluene-*p*-sulphonate (90 mg.) in ether (10 ml.) was heated overnight with lithium aluminium hydride (250 mg.). Filtration of a pentane solution of the product through aluminium oxide followed by removal of the solvent gave B-nor-5α-cholestane,

m. p. 78—79° (needles from acetone), $[\alpha]_D$ +9° (*c* 0·9) (Found: C, 87·1; H, 13·0. $C_{26}H_{46}$ requires C, 87·1; H, 12·9%].

(*b*) B-Nor-5α-cholest-2-ene (105 mg.) in ether (5 ml.) and acetic acid (5 ml.) was hydrogenated in the presence of platinum oxide (20 mg.). The product crystallised from acetone to give B-nor-5α-cholestane as needles, m. p. 78—80°.

B-*Nor*-5α-*cholestan*-3-*one*.—B-Nor-5α-cholestan-3β-ol (312 mg.) in pyridine (6 ml.) was treated with chromium trioxide (400 mg.) and left overnight. After dilution with pentane the solution was filtered and the filtrate evaporated under reduced pressure. The crystalline product was chromatographed on aluminium oxide (10 g.). Elution with benzene–pentane (1 : 4) gave B-*nor*-5α-*cholestan*-3-*one*, m. p. 98—99° (from methanol), $[\alpha]_D$ +25·5° (*c* 0·75), $\nu_{max.}$ 1706 cm.$^{-1}$ (in carbon tetrachloride) (Found: C, 83·5; H, 12·0. $C_{26}H_{44}O$ requires C, 83·8; H, 11·9%). Rotatory dispersion in methanol (*c* = 0·1): [*M*] = 0 at 600 mμ; +3470 at 310 mμ (peak); −3790 at 260 mμ.

Reduction of the ketone with lithium aluminium hydride in ether gave in quantitative yield B-nor-5α-cholestan-3β-ol, m. p. and mixed m. p. 130—131° (from methanol), $[\alpha]_D$ −10° (*c* 0·96).

B-*Nor*-5α-*cholestan*-3α-*ol*.—B-Nor-5α-cholestan-3β-yl toluene-*p*-sulphonate (850 mg.) in benzene was adsorbed on basic aluminium oxide (Woelm) and left for one week. Elution with pentane gave B-*nor*-5α-*cholest*-2-*ene* (326 mg.), m. p. 82—84° (plates from acetone), $[\alpha]_D$ +30·6° (*c* 1·5) (Found: C, 87·4; H, 12·1. $C_{26}H_{44}$ requires C, 87·6; H, 12·4%). Elution with chloroform gave B-*nor*-5α-*cholestan*-3α-*ol* (225 mg.), m. p. 124—127° (needles from acetone), $[\alpha]_D$ −24° (*c* 1·07) (Found: C, 83·5; H, 12·1. $C_{26}H_{46}O$ requires C, 83·35; H, 12·4%). Admixture with B-nor-5α-cholestan-3β-ol gave m. p. 116—119°.

The author thanks Dr. W. Klyne for the rotatory-dispersion data and Mr. D. Jones for the infrared spectra.

CHEMISTRY DEPARTMENT, UNIVERSITY COLLEGE OF WALES, SWANSEA.

[*Received, February 2nd,* 1959.]

---

583. *Heats of Formation and Bond Energies. Part I. Trisdiethylaminophosphine.*

By P. A. FOWELL and C. T. MORTIMER.

The heat of reaction between an excess of diethylamine and phosphorus trichloride in cyclohexane, to give trisdiethylaminophosphine, has been measured, *viz.*, $\Delta H_f^\circ[(Et_2N)_3P, liq.] = -66{\cdot}8 \pm 2{\cdot}5$ kcal./mole. The mean bond energy term, $\bar{E}(P{-}N) = 66{\cdot}8 \pm 0{\cdot}8$ kcal./mole, is derived. Also the value $\Delta H_f^\circ(Et_2NH,HCl, cryst.) = -85{\cdot}6 \pm 0{\cdot}2$ kcal./mole is found.

THE purposes of this series of papers are to report the measurement of heats of formation of compounds, from these to derive bond-energy terms and bond-dissociation energies, and to investigate deviation of these quantities from additivity. The first group to be considered are organophosphorus compounds, and this paper deals with a compound containing phosphorus–nitrogen bonds.

Recent papers on the thermochemistry of phosphorus compounds have dealt mainly with phosphorus–carbon,[1] phosphorus–oxygen,[2] and phosphorus–halogen[3,4] bonds in tervalent phosphorus compounds, and in phosphoryl and thiophosphoryl compounds with the effects of different groups bonded to the phosphorus atom.[5-8]

[1] Long and Sackmann, *Trans. Faraday Soc.*, 1957, **53**, 1606.
[2] Chernick, Skinner, and Mortimer, *J.*, 1955, 3936.
[3] Charnley and Skinner, *J.*, 1953, 450.
[4] Neale and Williams, *J.*, 1952, 4535; 1954, 2156.
[5] Chernick and Skinner, *J.*, 1956, 1401.
[6] Neale and Williams, *J.*, 1955, 2485.
[7] *Idem*, *J.*, 1956, 422.
[8] Chernick, Pedley, and Skinner, *J.*, 1957, 1851.

XUM

There is little thermochemical information about tervalent organophosphorus compounds containing phosphorus–nitrogen bonds, although for quinquevalent compounds the heats of formation of two alkylphosphonic dianilides are known.[7]

In an inert solvent, at room temperature, phosphorus trichloride reacts with a secondary amine, present in excess, to give an aminophosphine.[9] In cyclohexane, diethylamine reacts thus:

$$PCl_3(liq.) + 6Et_2NH(soln.) \longrightarrow (Et_2N)_3P(soln.) + 3Et_2NH,HCl(cryst.) \quad . \quad (1)$$

to give trisdiethylaminophosphine in solution and a precipitate of crystalline diethylamine hydrochloride.

With phosphorus oxychloride, triamino-derivatives are formed by reaction with secondary amines only at elevated temperatures.[10] At room temperature, in an inert solvent, one or two of the chlorine atoms are replaced by amino-groups. In cyclohexane, reaction with diethylamine gives a mixture of dichlorodiethylaminophosphine oxide and chlorobisdiethylamidophosphine oxide, and the reaction was found to be unsuitable for thermochemical study.

A secondary, rather than a primary, amine was chosen so as to avoid complication due to the possible formation of imides R·N=P·NHR [11] and R·N=PO·NHR.[12]

Experimental

Materials.—Cyclohexane (Howard, Ilford) was distilled, in dry nitrogen, from calcium hydride, immediately before use. Phosphorus trichloride (B.D.H. Laboratory Reagent) was distilled, in dry nitrogen, through a 6″ Fenske column, and had b. p. 74·4—74·6°/746 mm. It was redistilled *in vacuo* and sealed in thin, weighed glass phials. Diethylamine (B.D.H. Laboratory Reagent) was distilled, from calcium hydride, through an 18″ Fenske column; it had b. p. 54·7°/750 mm.

Trisdiethylaminophosphine was prepared by the addition of phosphorus trichloride (60 g., 0·42 mole) in ether (200 ml.) to diethylamine (210 g., 3·0 moles) in ether (1·5 l.). The precipitated amine hydrochloride was removed by filtration, then the ether by distillation, and the triaminophosphine was distilled under reduced (nitrogen) pressure, through a 6″ Fenske column. It had b. p. 85·0°/2 mm. Michaelis [10] gives b. p. 80—90°/10 mm.

Calorimeter.—The heats of reaction were measured in a calorimeter similar to that described by Pedley *et al.*[13]. It consisted of a cylindrical, silvered Dewar vessel (capacity 300 ml.) encased in a brass can fitted with a flanged brass lid, which was totally immersed in a thermostat bath at 25·000° ± 0·005°. Heavy brass chimneys in the calorimeter lid allowed entrance into the Dewar vessel of the stirrer (480 r.p.m.) and an electrical heater and thermistor element, both encased in glass tubes, and a glass rod holding a phial of reactant. The whole system, together with electrical equipment, was housed in a constant-temperature room at 25·0° ± 0·2°. The Dewar vessel was charged with a solution of diethylamine (39·5 g.) in cyclohexane (145·0 g.) which was kept under a slight positive pressure of dry nitrogen, to prevent ingress of moisture. When a steady state was reached thermally, the phial of phosphorus trichloride was crushed. With a molar ratio of PCl_3 : Et_2NH of 1 : 10 the reaction still continued after 60 min. The mole ratio used was 1 : 200, the reaction being complete in ~15 min. The calorimeter was calibrated electrically by the substitution method.

Units.—Heat quantities are given in units of the thermochemical calorie, 1 cal. = 4·1840 abs. joule.

Results.—In the reactions with phosphorus trichloride the precipitated diethylamine hydrochloride was recovered, in amount at least 99·8% of that required by reaction (1).

[9] Kosolapoff, " Organo-phosphorus Compounds," Chapman and Hall, Ltd., London, 1950, p. 278.
[10] Michaelis, *Annalen*, 1903, **326**, 129.
[11] Grimmel, Guenther, and Morgan, *J. Amer. Chem. Soc.*, 1946, **68**, 539.
[12] Michaelis, *Annalen*, 1915, **407**, 290; Michaelis and Silberstein, *Ber.*, 1896, **29**, 716.
[13] Pedley, Skinner, and Chernick, *Trans. Faraday Soc.*, 1957, **53**, 1612.

In Table 1, ΔH refers to the observed heat of reaction (1): the mean value is $-103{\cdot}2 \pm 1{\cdot}3$ kcal./mole. The comparatively large standard deviation is attributed to the formation of a precipitate, which may lead to heterogeneity in the final reaction mixture. Heats of solution

TABLE 1.

PCl_3 (g.)	0·2746	0·2804	0·2853	9·2666	0·2650	0·2969	0·2529	0·2694
$-\Delta H$ (kcal./mole)	99·5	108·0	102·1	103·6	108·2	100·2	102·7	101·3

in cyclohexane–diethylamine solution were measured independently, being Et_2NH(liq.) + $0{\cdot}44 \pm 0{\cdot}03$, and $(Et_2N)_3P$(liq.) $0 \pm 0{\cdot}05$ kcal./mole. With these additional data, the heat is calculated to be $\Delta H_2 = -100{\cdot}6 \pm 1{\cdot}5$ kcal./mole for the idealised reaction (2):

$$PCl_3(liq.) + 6Et_2NH(liq.) \longrightarrow (Et_2N)_3P(liq.) + 3Et_2NH,HCl(cryst.) \quad . \quad . \quad (2)$$

Heats of Formation.—The heat of formation of the aminophosphine is related to the corresponding ΔH_2 through the thermochemical equation:

$$\Delta H_f^\circ[(Et_2N)_3P, liq.] = \Delta H_2 + \Delta H_f^\circ(PCl_3, liq.) - 3\Delta H_f^\circ(Et_2NH,HCl, cryst.) + 6\Delta H_f^\circ(Et_2NH, liq.)$$

The value $\Delta H_f^\circ(PCl_3, liq.) = -74{\cdot}4$ kcal./mole (ref. 4) is accepted here, together with $\Delta H_{vap.} = 7{\cdot}8$ kcal./mole (ref. 14), which gives $\Delta H_f^\circ(PCl_3, g.) = -66{\cdot}6$ kcal./mole. A recent determination of the heat of combustion of liquid diethylamine [15] gives $\Delta H_c^\circ = -727{\cdot}2 \pm 0{\cdot}3$ kcal./mole, and with the usual values, $\Delta H_f^\circ(H_2O, liq.) = -68{\cdot}3174$ and $\Delta H_f^\circ(CO_2, g.) = -94{\cdot}0518$ kcal./mole,[14] gives $\Delta H_f^\circ(Et_2NH, liq.) = -24{\cdot}8 \pm 0{\cdot}3$ kcal./mole. [Incorporating the latent heat of vaporisation, $\Delta H_{vap.} = 7{\cdot}8$ kcal./mole, obtained from Jordan's vapour pressure data,[16] we calculate $\Delta H_f^\circ(Et_2NH, g.) = -17{\cdot}0$ kcal./mole.]

The heat of formation of crystalline diethylamine hydrochloride was determined by two methods. In the first, diethylamine was dissolved in excess of 0·2N-hydrochloric acid:

$$Et_2NH(liq.) + HCl\ (223H_2O) + \text{Excess of acid solution} \longrightarrow Et_2NH,HCl\ (\text{in acid solution})$$
$$\Delta H = -20{\cdot}50 \pm 0{\cdot}10 \text{ kcal./mole}$$

The heat of solution of crystalline diethylamine hydrochloride in excess of 0·2N-hydrochloric acid was also measured:

$$Et_2NH,HCl(cryst.) + \text{Excess of acid solution} \longrightarrow Et_2NH,HCl\ (\text{in acid solution})$$
$$\Delta H = +0{\cdot}65 \pm 0{\cdot}03 \text{ kcal./mole}$$

Whence, by using $\Delta H_f^\circ(HCl,223H_2O) = -39{\cdot}81$ kcal./mole [14] and $\Delta H_f^\circ(Et_2NH, liq.)$ derived above, $\Delta H_f^\circ(Et_2NH,HCl, cryst.) = -85{\cdot}76 \pm 0{\cdot}33$ kcal./mole.

In the second method diethylamine hydrochloride was dissolved in excess of 0·2N-sodium hydroxide:

$$Et_2NH,HCl(cryst.) + NaOH(223H_2O) + \text{Excess of alkali} \longrightarrow (Et_2NH + NaCl + H_2O)\ (\text{in alkaline solution})$$
$$\Delta H = -0{\cdot}33 \pm 0{\cdot}03 \text{ kcal./mole}$$

The heat of solution of liquid diethylamine in excess of 0·2N-sodium hydroxide was also measured:

$$Et_2NH(liq.) + \text{Excess of alkaline solution} \longrightarrow Et_2NH\ (\text{in alkaline solution})$$
$$\Delta H = -7{\cdot}53 \pm 0{\cdot}05 \text{ kcal./mole.}$$

The following additional data are used:

[14] National Bureau of Standards, Circular 500, Washington, D.C., 1952.
[15] Prosen, National Bureau of Standards, Washington D.C., personal communication.
[16] Jordan, "Vapor Pressure of Organic Compounds," Interscience Publ. Inc., London, 1954, p. 179.

XUM

$\Delta H_f°(NaOH,223H_2O) = -112{\cdot}10$, and $\Delta H_f°(NaCl,223H_2O) = -97{\cdot}21$ kcal./mole:[14] here the assumption is made that the heat of solution of crystalline sodium chloride to this dilution is the same in water as in 0·2N-sodium hydroxide. From these data we calculate $\Delta H_f°(Et_2NH,HCl, cryst.) = -85{\cdot}42 \pm 0{\cdot}38$ kcal./mole. The two methods give results in close agreement, which serves as a check on the calibration of the calorimeter. We take $\Delta H_f°(Et_2NH,HCl, cryst.) - \Delta H_f°(Et_2NH, liq.) = -60{\cdot}80 \pm 0{\cdot}15$ kcal./mole.

From these data and ΔH_2, we derive $\Delta H_f°[(Et_2N)_3P, liq.] = -66{\cdot}8 \pm 2{\cdot}5$ kcal./mole.

The vapour pressure of this compound has been measured and is given by the equation $\log_{10} p(mm.) = -A/T + B$, where $A = 3171$ and $B = 8{\cdot}80$. The derived latent heat of vaporisation (liquid to vapour), given by $\Delta H_{vap.} = -4{\cdot}57A \times 10^{-3}$ kcal./mole, is $14{\cdot}5 \pm 0{\cdot}1$ kcal./mole.

Incorporating these values gives $\Delta H_f°[(Et_2N)_3P, g.] = -52{\cdot}3 \pm$ kcal./mole.

Discussion

The first step in deriving bond-energy terms is to calculate the heat of formation of the gaseous compound from the atoms, $\Delta H_f^a(g.)$.

This may be obtained from the relation:

$$\Delta H_f^a(g.) = \Delta H_f°(g.) - \Sigma \Delta H_a,$$

where $\Delta H_f°(g.)$ is the heat of formation of the gaseous compound from the elements and the ΔH_a terms are the heats of atomisation of the elements at 25°. Values used are: C, 170·89;[17] H, 52·09;[14] O, 59·54; N, 112·9; P, 75·3; and Cl, 28·94 kcal./g.-atom.[18]

From the $\Delta H_f°(g.)$ values above and $\Delta H_f°(POCl_3, g.) = -134{\cdot}3$ kcal./mole (ref. 3), the $\Delta H_f^a(g.)$ terms are calculated: PCl_3, −228·72; $POCl_3$, −355·96; $(Et_2N)_3P$, −4079·7; and Et_2NH, −1386·45 kcal./mole. The group energy term, $\bar{E}(Et_2N)$, the sum of the bond-energy terms in the group, is evaluated from $\bar{E}(Et_2N) = -\Delta H_f^a(Et_2NH, g.) - \bar{E}(N{-}H)$. Taking $\bar{E}(N{-}H) = 93{\cdot}4$ kcal./mole we have $\bar{E}(Et_2N) = 1293{\cdot}05$ kcal./mole. Since $\Delta H_f^a[(Et_2N)_3P, g.] = 3\bar{E}(Et_2N) + 3\bar{E}(P{-}N)$, we derive $\bar{E}(P{-}N) = 66{\cdot}8 \pm 0{\cdot}8$ kcal./mole. Also, since $-\Delta H_f^a(PCl_3, g.) = 3\bar{E}(P{-}Cl)$, we obtain $\bar{E}(P{-}Cl) = 76{\cdot}2$ kcal./mole.

For phosphoryl compounds the situation is less simple. It has been suggested[5] that the OPR_3 molecule should be regarded as a tetrahedral structure, $^-O{-}{}^+PR_3$, modified by back co-ordination from the $2p_x$ and $2p_y$ orbitals of O^- to the vacant $3d_\pi$ orbitals of P^+, thus giving $^-O{-}P^+$ triple-bond character, with the further possibility of back co-ordination to P from the R atoms or groups if these have donor electrons.

Oxidation of the compound PR_3 to OPR_3 is accompanied by a number of energy changes. (i) The promotional energy of the phosphorus atom from the tervalent to the quinquevalent state. (ii) The energy of formation of the phosphoryl bond, which is not constant from one molecule to another, as suggested by the shift in the Raman frequency and infrared wavelength of the phosphoryl bond, on changing the R groups.[19] (iii) The energy change accompanying alteration in the P–R bond character, *e.g.*, as indicated by a shortening of the P–Cl bond length of 2·04 Å, in phosphorus trichloride,[20] to 1·99 Å in phosphorus oxychloride,[21] suggesting a strengthening of this bond on oxidation.

A measure of the energy changes on oxidation is the heat of dissociation, $D(P{=}O)$, of the molecule OPR_3 in the gaseous state, $OPR_3(g.) \longrightarrow O(g.) + PR_3(g.)$. It is given by the thermochemical equation:

$$D(P{=}O) = \Delta H_f°(PR_3, g.) - \Delta H_f°(OPR_3, g.) + \Delta H_f°(O, g.)$$

[17] Brewer and Searcy, *Ann. Rev. Phys. Chem.*, 1956, **7**, 259.
[18] Cottrell, "The Strengths of Chemical Bonds," Butterworths Scientific Publications, London, 2nd Edn., 1958.
[19] Williams, Gordy, and Sheridan, *J. Chem. Phys.*, 1952, **20**, 164.
[20] Kisliuk and Townes, *Phys. Rev.*, 1950, **78**, 347.
[21] Bell, Heisler, Tannenbaum, and Goldenson, *J. Amer. Chem. Soc.*, 1954, **76**, 5185.

and is a quantity of physical significance in that, at least in theory, it is capable of direct measurement. For phosphorus oxychloride we have $D(P{=}O) = 127{\cdot}2$ kcal./mole. Similarly, from $\Delta H_f°(P_4O_6, g.)$ and $\Delta H_f°(P_4O_{10}, g.)$, the value $D(P{=}O) = 115$ kcal./mole has been calculated.[6] Although $\Delta H_f°[(Et_2N)_3P, g.]$ is known, the corresponding $\Delta H_f°[(Et_2N)_3PO, g.]$ is unknown, and $D(P{=}O)$ cannot be obtained in this case.

An alternative, though less fundamental, approach is to calculate bond-energy terms, and this depends on apportioning the total energy change on oxidation. Here the energy changes (i) and (ii) are assumed to be constant from one molecule to another, identified with the bond-energy term, $\bar{E}(P{=}O)$, and given an arbitrary value of 115·0 kcal./mole.[6] From the relation $-\Delta H_f^a(POCl_3, g.) = 3\bar{E}(P{-}Cl) + \bar{E}(P{=}O)$, we calculate $\bar{E}(P{-}Cl) = 80{\cdot}3$ kcal./mole, some 4·1 kcal./mole greater than for this bond in phosphorus trichloride. Neale and Williams [6] have previously calculated $\bar{E}(P{-}Cl) = 80$ kcal./mole, in phosphorus oxychloride, using slightly different heats of atomisation given in N.B.S. Circular 500.[14]

Neale and Williams [7] measured the heat of the reaction between alkylphosphonic dichlorides and aniline, in cyclohexane solution, and derive the following thermochemical relation:

$$\Delta H_f°(MePOCl_2, cryst.) - \Delta H_f°[MePO(Ph{\cdot}NH)_2, cryst.] = -62{\cdot}2 \pm 1{\cdot}0$$

$$\Delta H_f°(EtPOCl_2, liq.) - \Delta H_f°[EtPO(Ph{\cdot}NH)_2, cryst.] = -57{\cdot}7 \pm 1{\cdot}0 \text{ kcal./mole.}$$

If it can be assumed that the latent heats of sublimation of the dichloride and corresponding dianilide are the same within ±1·0 kcal./mole, as seems likely, and that $\Delta H_{fusion}(EtPOCl_2) = 3{\cdot}0$ kcal./mole, then we calculate

$$\Delta H_f^a(MePOCl_2, g.) - \Delta H_f^a[MePO(PhNH)_2, g.] = +2781{\cdot}5$$

$$\Delta H_f^a(EtPOCl_2, g.) - \Delta H_f^a[EtPO(PhNH)_2, g.] = +2783{\cdot}0 \text{ kcal./mole.}$$

From the relation:

$$\Delta H_f^a(MePOCl_2, g.) - \Delta H_f^a[MePO(PhNH)_2, g.] = 2\bar{E}(Ph{\cdot}NH) + 2\bar{E}(P{-}N) - 2\bar{E}(P{-}Cl),$$

the bond-energy term $\bar{E}(P{-}N)$ may be calculated in terms of $\bar{E}(P{-}Cl)$. The group energy term, $\bar{E}(Ph{\cdot}NH) = 1389{\cdot}1$ kcal./mole, is evaluated from $\bar{E}(PhNH) = -\Delta H_f^a(Ph{\cdot}NH_2, g.) - \bar{E}(N{-}H)$, by taking $\Delta H_f^a(Ph{\cdot}NH_2, g.) = -1482{\cdot}5$ kcal./mole. This is derived from $\Delta H_f°(PhNH_2, g.) = +20{\cdot}4$ kcal./mole, calculated in turn from $\Delta H_c°(Ph{\cdot}NH_2, g.) = -823{\cdot}8$ kcal./mole (ref. 22).

Taking $\bar{E}(P{-}Cl) = 80{\cdot}3$ kcal./mole, as in phosphorus oxychloride, we obtain $\bar{E}(P{-}N) = 82{\cdot}0 \pm 2{\cdot}0$ and $82{\cdot}5 \pm 2{\cdot}0$ kcal./mole, where R = Me and Et, respectively. These values are some 15—16 kcal./mole greater than in the aminophosphine.

TABLE 2.

Bond	Tervalent Compound	$\bar{E}$(P–R)	Phosphoryl * Compound	$\bar{E}$(P–R)	$\Delta\bar{E}$
P–F	PF_3	117·0 † ‡	POF_3	121·9 ‡	4·9
P–Cl	PCl_3	76·2 [4]	$POCl_3$	80·3 [3]	4·1
P–Br	PBr_3	61·7 [3]	$POBr_3$	65·0 [3]	3·3
P–OR	$(EtO)_3P$	91·9 [3]	$(EtO)_3PO$	103·8 [5]	11·9
	$(Pr^iO)_3P$	92·3 [6]	$(Pr^iO)_2P(O)Me$	102·9 [6]	10·6
P–N	$(Et_2N)_3P$	66·8	$(Ph{\cdot}NH)_2P(O)Me$	82·0 [7]	15·2
			$(Ph{\cdot}NH)_2P(O)Et$	82·5 [7]	15·7

* $\bar{E}(P{=}O)$ being taken as 115·0 kcal./mole. † Refs. are to heats of formation from which $\bar{E}(P{-}R)$ is derived. ‡ Ebel and Bretscher, *Helv. Chim. Acta*, 1929, **12**, 450.

In Table 2 are to be found some bond-energy terms, together with the difference in these terms, $\Delta\bar{E}$, for a particular bond, in phosphoryl and in tervalent phosphorus compounds. Down the series P–F, P–Cl, P–Br, the $\Delta\bar{E}$ values decrease slightly from 4·9 to 3·3 kcal./mole,

[22] Klages, *Chem. Ber.*, 1949, **82**, 358.

which runs parallel to a decrease in electronegativity [23] from 3·9 (F) through 3·0 (Cl) to 2·8 (Br). Along the series P–F, P–O, P–N, the $\Delta\bar{E}$ values increase considerably from ~5 through ~11 to ~16 kcal./mole, despite a similar decrease in electronegativity to 3·0 for nitrogen. It seems likely that bond strengthening is due to back-co-ordination to the phosphorus atom.

In the series of compounds, $(Me_2N)_nBCl_{3-n}$ and $(EtO)_nBCl_{3-n}$, it has been shown [24] that bond strengthening, due to back-co-ordination to the boron, is very much greater from nitrogen than from oxygen, which is, in turn, greater than from chlorine. This same order is also found in phosphorus compounds.

One of us (P. A. F.) thanks the Distiller's Co. Ltd. for a maintenance grant.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE,
KEELE, STAFFS.

[*Received, March 9th,* 1959.]

[23] Pritchard and Skinner, *Chem. Rev.*, 1955, **55**, 745.
[24] Skinner and Smith, *J.*, 1954, 3930.

---

584. *Hydrogenation of Oximes with Platinum Metal Catalysts.*

By EDITH BREITNER, ELEANOR ROGINSKI, and PAUL N. RYLANDER.

The rate of hydrogenation of cyclohexanone oxime in presence of various platinum catalysts in several solvents has been determined. The course of the hydrogenation is discussed.

THIS paper deals with the low-pressure hydrogenation of oximes in presence of palladium, platinum, rhodium, and ruthenium on carbon of high surface area. Low-pressure hydrogenation of oximes has been reported only infrequently [1] and confined mainly to Raney nickel catalysts. No report comparing the rate of reduction of an oxime by various platinum metal catalysts has been made.

In Table 1 the rates of hydrogenation of cyclohexanone oxime in various solvents are given. All reactions were continued, except when the rate was very slow, until two mols. of hydrogen had been absorbed, whereupon the reaction generally ceased abruptly. No cyclohexane was formed under the conditions used, except in methanol. With a few interesting exceptions the rates were of zero order over almost the entire reaction, or in very slow reactions, over the smaller range examined. This order implies a simplicity

TABLE 1. *Rate of hydrogenation* (*ml. of* H_2 *per min.*) *of cyclohexanone oxime* (400 *mg.*) *in various solvents* (100 *ml.*) *with various catalysts* (300 *mg.*) *at* 25°.

Solvent	5% Pd	5% Rh	5% Ru	5% Pt
AcOH	0·5	1·9	0·2	8·0
Water	0·5	10·2	1·5, 5·2 *	†
0·5M-NaOH, aq.	0·5	22·8	3·2, 8·0 *	†
0·5M-HCl, aq.	0·45	2·1	0·2	24·0
Methanol	0·7	5·3	0·3	0·7
Dioxan	0	0	0	0

* The first and second portion respectively of the hydrogenation.
† Catalyst poisoned rapidly.

that does not, in fact, exist. In water, the major product is cyclohexanol and not cyclohexylamine. Despite the complexity of the reaction, the observed rate must be the rate of reduction of the oxime, and not of some intermediate product. The alcohol arises by hydrolysis of the imine and not by hydrolysis of the oxime and reduction of the ketone. Oximes are hydrolysed very slowly in water,[2] and in the time required for complete reduction

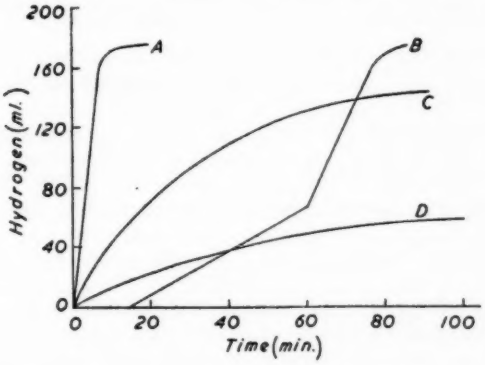
[1] Iffland and Teh-Fu Yen, *J. Amer. Chem. Soc.*, 1954, **76**, 4180; Buckley, *J.*, 1947, 1494.
[2] Taylor and Baker, "Sidgwick's Organic Chemistry of Nitrogen," Oxford Univ. Press, 1937.

no measurable amount of hydroxylamine, determined by titration, is formed. Cyclohexanol was not formed by catalytic dehydrogenation of cyclohexylamine to the imine,[3] for under the conditions of the experiments cyclohexylamine was recovered unchanged.

The effect of solvent on reaction rate is marked. Dioxan, a solvent frequently used for high-pressure reductions, is worthless at low pressures. In methanol the rate is convenient only when rhodium is the catalyst, and in acetic acid only when it is platinum.

In methanol a slow, partial hydrogenolysis occurred that ceased before the third mol. of hydrogen was absorbed. Cyclohexyl alcohol and cyclohexylamine both resisted hydrogenolysis under the conditions employed. Cyclohexanone ketal, a probable product of the reaction, did undergo a slow hydrogenolysis. Although ketones do not usually form ketals under these conditions,[4] cyclohexanone (and probably its imine) form a ketal readily with methanol.[5]

The rate of hydrogenation in water is sharply dependent on pH, except with palladium catalysts. In neutral solution hydrogenation with platinum begins fast but becomes



Hydrogenation of cyclohexanone oxime.
A, Pt *in* 0·6N-HCl.
B, Ru *in* H_2O.
C, Pt *in* H_2O.
D, Pt *in* H_2O plus *cyclohexylamine*.

slower and virtually ceases after 75% of the theoretical absorption. The decline in rate is probably due to poisoning by cyclohexylamine. In acid solution, where the amine could be converted into the ammonium salt, the reaction is fast and of zero order. The rate curve was virtually unchanged when 400 mg. of cyclohexylamine hydrochloride were added initially, but the catalyst was poisoned immediately when 300 mg. of the free amine were added (see Figure). A similar observation has been made with hydrogenation of unsaturated amines over platinic oxide.[6]

The activity of a rhodium catalyst is also affected greatly by pH, but the reason is less clear in this case. The absorption rate changes from 2·1 ml./min. in 0·5N-hydrochloric acid to 22·8 ml./min. in 0·5N-sodium hydroxide. Oximes behave as both acids and bases,[3] and the change in rate may reflect a change in the structure of the ion undergoing reduction. A parallel, though smaller, change in rate with pH has been observed in the reduction of nitrobenzene with rhodium,[7] and it was suggested then, to account for this pH dependence, that rhodium ionizes hydrogen heterolytically.

Palladium catalysts show very little variation in rate with changing environment, and in no case are they particularly active for reduction of oximes. The rate of reduction of nitrobenzene by palladium, very fast, is also insensitive to pH, which led to the suggestion [7] that palladium, unlike rhodium, ionizes hydrogen homolytically.

[3] Yura, Nakao, and Goto, *J. Chem. Soc. Japan*, 1952, **55**, 337.
[4] Post, "The Chemistry of Aliphatic Orthoesters," ACS Monograph 92, Reinhold Publ. Corp., New York, 1943, chapter 3.
[5] McCoy, Baker, and Gohlke, *J. Org. Chem.*, 1957, **22**, 1175.
[6] Devereux, Payne, and Peeling, *J.*, 1957, 2845.
[7] Hernandez and Nord, *Experientia*, 1947, **3**, 12.

XUM

Ruthenium catalysts exhibit a rather unusual rate curve (see Figure). The rate is essentially of zero order until reaction is about 60% complete, then the curve changes abruptly to a faster zero-order one. This reaction was repeated six times with varying ratios of catalyst to substrate and with different catalysts. The break-point always occurred at 60—63% completion. Sometimes, but not always, there was an initial induction period, as indicated in the Figure. Once this induction period lasted 180 minutes. Variable, and occasionally lengthy, induction periods are characteristic of the ruthenium catalyst and have caused many excellent ruthenium catalysts to be discarded. There seems to be no correlation between the length of the induction period and the rate of hydrogenation (unpublished results from our laboratories).

Although most of the reductions lead to zero-order rate curves, hydrolysis occurs concomitantly with hydrogenation and cyclohexanol usually predominates in the products. In Table 2 the yield of cyclohexylamine in various solvents is given. Those conditions that lessen the opportunity for hydrolysis of imine give increased yields of amine. Ammonia has been used previously to increase the yield of primary amine at the expense of secondary amine,[8] but in the present work its beneficial effect seems to arise mostly

TABLE 2. *Yield* (%) *of cyclohexylamine formed from cyclohexanone oxime* (10 *g.*) *in various solvents with rhodium catalysts* (5 *g.*; 5% *on carbon*).

Solvent	Yield	Solvent	Yield
Water, 400 ml.	25	Methanol, 100 ml.	48
0·125M-NaOH, 400 ml.	29	Ethanol, 100 ml.	55
Conc. aq. NH_3, 400 ml.	77	Methanol, saturated with NH_3, 100 ml.	82

from its competition with water in nucleophilic attack on the imine: $X{:}NH + NH_3 \longrightarrow X(NH_2)_2 \xrightarrow{H_2} NH_3 + X\langle_{NH_2}^{H}$. The yield of secondary amine was in all cases less than a few per cent. Surprisingly, the yield of secondary amine seemed equally as large in the dilute solutions of the kinetic experiments, during which the dicyclohexylamine formed a complex with cyclohexanol and floated on top of the solution as white flakes, m. p. 48°.[9] The lack of dependence of yield of secondary amine on the concentration of the reactants suggests that alkylation occurs on a saturated catalyst surface. This suggestion has been made to account for the fact that in the hydrogenation of nitriles the yield of secondary amine is increased only slightly by prior addition of primary amine to the nitrile solution.[10]

EXPERIMENTAL

The catalysts were commercial preparations manufactured by Engelhard Industries of 5% reduced metal on carbon of high surface area (Norit). Ruthenium catalysts were reduced immediately before use by shaking them in solvent under hydrogen (1 atm.) for 1 hr., after which the flask was flushed with nitrogen and the substrate added. The other catalysts were used directly as received. Electrolytic hydrogen and " reagent grade " solvents were used without further purification. Cyclohexanone oxime, m. p. 88°, was purified by recrystallization from ethanol.

In the rate measurements, the hydrogen consumption was measured over a small change in pressure by a differential manometer with sensitive strain gauges and an electronic recording potentiometer. Rate measurements were made at room temperature and an initial pressure of 1 atm. with 300 mg. of catalyst, 400 mg. of substrate, and 100 ml. of solvent. During the experiment the pressure fell 5—10%. Agitation by shaking was sufficiently vigorous to eliminate contribution of hydrogen transport to the reaction rates.

ENGELHARD INDUSTRIES RESEARCH LABORATORIES,
NEWARK, NEW JERSEY, U.S.A.

[*Received, March 9th,* 1959.]

[8] Reeve and Christian, *J. Amer. Chem. Soc.*, 1956, **78**, 860.
[9] Winans, *ibid.*, 1939, **61**, 3591.
[10] Juday and Adkins, *J. Amer. Chem. Soc.*, 1955, **77**, 4559.

585. *The Biosynthesis of Ricinine.**

By HADASSAH TAMIR and DAVID GINSBURG.

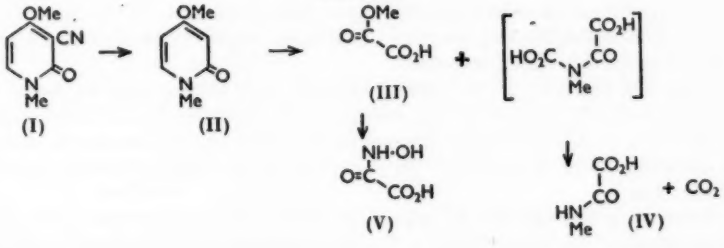
[2-^{14}C]Lysine hydrochloride, fed hydroponically to seedlings of *Ricinus communis* L., is incorporated in the ricinine produced by the plant. An ozonolytic procedure, which was developed in order to degrade 4-methoxy-1-methyl-2-pyridone formed from the labelled ricinine, showed that the latter is labelled solely in one position, α to the ring-nitrogen atom. Alternatively, α-amino[ε-^{14}C]adipic acid, similarly fed to the same plant, is also incorporated in the ricinine produced. In this case, however, both positions α to the ring-nitrogen atom were equally labelled in the alkaloid. These results are discussed.

FOR the first in a series of studies on the biosynthesis of alkaloids in plants, *Ricinus communis* L. which produces *ca.* 1% (dry weight) of a single alkaloid, ricinine [1] (I), was selected.

Seeds of this plant were permitted to sprout in the dark, the seedlings were transferred to a container in which the roots dipped into an aqueous solution of DL-[2-^{14}C]lysine hydrochloride and were grown for 14 days under controlled conditions. They were then harvested, dried, defatted (Soxhlet) with light petroleum, and then extracted (Soxhlet) with chloroform. After suitable working up, labelled ricinine was isolated.

Authentic ricinine was synthesised [2] and the unlabelled alkaloid was converted into 4-methoxy-1-methyl-2-pyridone (II) by heating it with 57% sulphuric acid at 140° for one hour.[3] Ozonolysis in ethyl acetate at −60° followed by oxidative decomposition with 30% hydrogen peroxide, then afforded three degradation products (scheme 1): methyl hydrogen oxalate (III), the *N*-methyloxamic acid (IV), and carbon dioxide. The last two substances are presumably formed from the unstable carbamic acid shown which is decarboxylated spontaneously. The carbon dioxide was isolated as barium carbonate (90% yield). Since the acid ester (III) could not be readily separated from the amidic acid (IV), the former was converted into hydroxyoxamic acid (V) under conditions which left the acid amide unaffected. The compounds (IV) and (V) were then isolated by paper chromatography in 85% and 65% yield, respectively.

Scheme 1.



The labelled ricinine produced by the plant was also converted into the pyridone (II) in yield (65%) similar to that from the unlabelled alkaloid.[3] The cyano-group was isolated in 97% yield as silver cyanide [4] and was shown to be unlabelled. Methoxyl and *N*-methyl

* A preliminary note has been published (Abs. Internat. Congr. Biochem., Vienna, September, 1958, p. 142).

[1] Tuson, *J.*, 1864, **17**, 195.
[2] Schroeter, Seidler, Sulzbacher, and Kanitz, *Ber.*, 1932, **65**, 432.
[3] Späth and Tschelnitz, *Monatsh.*, 1921, **42**, 251.
[4] Bottcher, *Ber.*, 1918, **51**, 673.

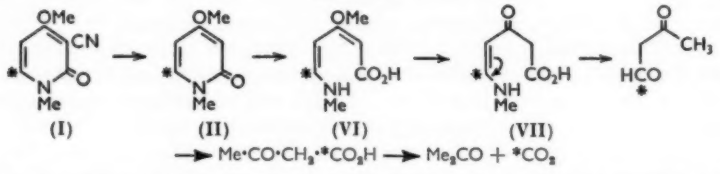
XUM

microdeterminations showed that no radioactivity resided at either the 1-methyl or the 4-methoxyl carbon atom. These methyl groups are known to be introduced into the ricinine molecule by methionine.[5]

Further, when the labelled pyridone (II) was ozonised, the hydroxylamine derivative (V) [produced from the acid ester (III)] and the acid amide (IV) were both unlabelled, and only the barium carbonate produced from the *non-carbonylic* α-carbon atom of the pyridone ring was labelled; its radioactivity fully accounted for that of the undegraded ring.

A complication, however, arose. The carbon dioxide formed by hydrolysis of the cyano-group [during the change (I) ⟶ (II)] was isolated as partially labelled barium carbonate. It appeared, at first, that this salt was labelled and thus, that the cyano-group of ricinine was partially labelled. This is clearly an artifact in view of the practically quantitative isolation of the cyano-group as unlabelled silver cyanide (see above). Indeed, 156% of the theoretical yield of barium carbonate was obtained from the transformation (I) ⟶ (II) so that it appears that unlabelled carbon dioxide resulting from hydrolysis of the cyano-group is diluted with radioactive carbon dioxide from the single labelled position in the ring. The latter labelled material is presumably formed from *ca.* 35% of the ricinine which is lost during the transformation (I) ⟶ (II) in a competitive reaction such as shown in the hypothetical reaction scheme 2.

Scheme 2.



It is here assumed that the " open " amino-acid (VI) formed during hydrolysis of ricinine under strongly acid conditions affords the β-oxo-acid (VII) which is both decarboxylated and hydrolysed as an enamine to afford formylacetone. This, by aerial oxidation, should give acetoacetic acid which on decarboxylation affords labelled carbon dioxide, diluting the unlabelled material from the cyano-group. Indeed, calculation of the radioactivity of this carbon dioxide, coupled with the specific activity and yield of the pyridone (II) and with the complete lack of radioactivity of the silver cyanide isolated in the alternative degradation procedure, justifies the conclusion that this carbon dioxide is, indeed, an artifact. The analogous degradations of ricinine formed from labelled α-aminoadipic acid further support this view (see below).

Since only one position in the ricinine, isolated after feeding with radioactive lysine, was labelled [scheme 2, (I) starred], the possibility presented itself that α-aminoadipic acid is an intermediate in the utilisation of lysine by the plant, through oxidative deamination of the ε-amino-group of the latter.[6] In a paper-chromatographic search this acid was indeed discovered.

In order to ascertain whether α-aminoadipic acid is formed from the lysine fed to the plant, this compound incorporating an ε-^{14}C atom was synthesised [6] and fed hydroponically to *Ricinus communis* L. This substance was incorporated by the plant more efficiently than lysine, and the labelled ricinine isolated was degraded as described above. In this case, only half of the radioactivity resided at the *non-carbonylic* α-carbon atom whilst the other half resided at the *carbonyl* carbon atom. The former conclusion was drawn in exact analogy to the result obtained for ricinine formed from lysine whilst the latter was drawn as follows: The hydroxy-amide (V) in this case was unlabelled, but the amide (IV) was labelled. The acid amide was submitted to the Schmidt reaction and 1·03 mol. of unlabelled

[5] Dubeck and Kirkwood, *J. Biol. Chem.*, 1952, **199**, 307.
[6] Borsook, Deasy, Haagen-Smit, Keighley, and Lowy, *J. Biol. Chem.*, 1948, **176**, 1383, 1395.

carbon dioxide were isolated. The reaction mixture was then diluted with water and heated in order to hydrolyse the *N*-methylurea (VIII) which is the product of the Schmidt reaction. The carbon dioxide thus obtained (0·97 mol.), corresponding to the carbonyl-carbon atom of ricinine, was labelled.

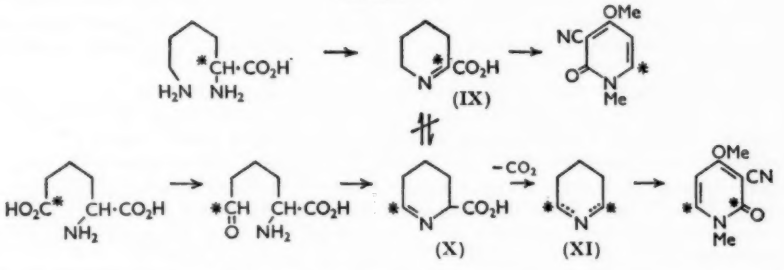
$$\underset{\text{(IV)}}{Me{\cdot}NH{\cdot}{}^{*}CO{\cdot}CO_2H} \longrightarrow \underset{\text{(VIII)}}{Me{\cdot}NH{\cdot}{}^{*}CO{\cdot}NH_2} + CO_2$$

$$\longrightarrow (Me{\cdot}NH_2)_2SO_4 + (NH_4)_2SO_4 + {}^{*}CO_2$$

The present type of study cannot clarify the exact nature and order of steps in the incorporation of lysine to afford ricinine. However, the unique incorporation of radioactive carbon into a single position within ricinine indicates that lysine is not broken up into small fragments, albeit the incorporation is only of about 1 part in 10,000.

The formation of αα′-doubly labelled ricinine from α-amino[ε-^{14}C]adipic acid renders untenable the hypothesis that the latter is formed from lysine by oxidative deamination of its ε-amino-group. This hypothesis would require the formation of carbonyl-labelled ricinine if α-aminoadipic acid were in fact an intermediate in lysine incorporation. However, the results obtained in this work fit into the known metabolic relationships between lysine and α-aminoadipic acid in *Neurospora* and in the rat.[7] They may be rationalised as in scheme 3.

Scheme 3.



This scheme presupposes that cyclisation of α-aminoadipic acid occurs at the aldehyde oxidation state or its equivalent and that no equilibrium exists within the plant between the acids (IX) and (X). Further, while the acid (IX) is oxidised at the unlabelled α-position and the product is transformed into ricinine through a series of as yet unelucidated steps, the acid (X) must be decarboxylated to a symmetrical intermediate (XI) which is then further transformed into ricinine.

Leete has shown that, although lysine is not a precursor of the pyridine ring of nicotine or of anabasine, it is the precursor of the piperidine ring of the latter.[8] This is a further indication that a more hydrogenated ring is formed from lysine by *Ricinus communis* L. and converted into the higher oxidation state of a substituted pyridone through a series of secondary transformations.

Even more relevant is Leete's clear-cut demonstration that a preformed pyridine derivative (nicotinic acid) is a precursor of ricinine in the plant.[9] [*carboxy*-^{14}C]Nicotinic acid afforded [*cyano*-^{14}C]ricinine.

In an attempt to find a connexion between them, labelled lysine and unlabelled nicotinic acid were fed simultaneously to sprouting seedlings of *Ricinus communis* L. This resulted in a two-fold increase in the yield of ricinine, compared with that obtained in absence of nicotinic acid. However, the specific activity was also higher by a factor of 2. This is

[7] Cf. Work, in " Amino Acid Metabolism," Johns Hopkins Press, Baltimore, 1955, pp. 468–469, and references therein.
[8] Leete, *J. Amer. Chem. Soc.*, 1956, **78**, 3520.
[9] Leete and Leitz, *Chem. and Ind.*, 1957, 1572.

not a significant increase in specific activity but it appears that the clarification of the relationship, if any, between these two precursors requires further investigation.

Experimental

Growth Experiments.—Seeds of *Ricinus communis* L. were treated with a solution made up of 1% aqueous mercuric chloride (3 parts by wt.) and ethanol (96%; 1 part by wt.) for 1 min. They were then transferred to pre-boiled water at 85° for 2 min. All parts of the equipment, water, and sand were sterilised.

The sterilised seeds were spread on sand in enamel trays (40 by 60 cm.) allowing 10 cm. between seeds. The trays were covered with plate glass and placed in a sterile dark cupboard at 27°, and the seeds were watered every 48 hr. Sprouting occurred *ca.* 5 days after " planting." The most well developed seedlings were transferred 10 days after " planting " to cylindrical glass jars (20 cm. diam.; 10 cm. high). Excess of sand was removed from the roots by rapid washing with sterile water. In order to avoid contact between the upper part of the plant and the aqueous solution into which the roots were dipped, the latter were drawn through 15 holes (0·75 cm. diam.) in a Perspex plate supported on several pegs 2 cm. from the bottom of the jar. The seedlings were watered through an opening in the cover of the jar, and sterile air was circulated during the whole growth-period. The seedlings grow to a height of *ca.* 20 cm. during 3 weeks. During this time the cotyledons emptied almost completely.

Feeding with Labelled Amino-acids.—The solution was added through the aeration inlet. Feeding was begun 2 weeks after " planting ". Two batches of DL-[2-^{14}C]lysine hydrochloride (Tracerlab, Inc.) were used in this work: (*a*) 55·3 mg. (0·1 mc) in the preliminary experiments; (*b*) 285 mg. (1 mc).

Lysine hydrochloride (20—80 mg.) was dissolved in sterile water (12 ml.), and portions (1 ml.) of this solution were added to each of two jars containing seedlings, during 6 days.

Isolation of Ricinine.—The seedlings were harvested 20 days after " planting." The roots were separated and discarded as they contain a negligible quantity of ricinine.[10] The rest of the plant material was dried at 95° and ground to a powder corresponding in weight to 31% of the living plant. The powder (20 g.) was extracted (Soxhlet) with light petroleum for 24 hr. The lipid concentration in the plant varies (8—13%) and depends upon the degree of emptying of the cotyledons.

The powder was dried at 95°, re-ground, and extracted with chloroform for 70 hr., the powder being broken up occasionally. (After development of this procedure, Leete and Leitz reported an almost identical procedure.) The extract was dried (Na_2SO_4), and the solvent was removed. Crystallisation of the yellow amorphous residue from ethanol and sublimation at 120°/0·01 mm. afforded colourless crystals (170 mg., 0·85%), m. p. 201°.

A more effective isolation procedure was found when ethanol-extraction (40 hr.) followed the defatting by light petroleum. Removal of the solvent afforded a brownish-red resin which was dissolved in water; a small insoluble portion was removed by filtration through cotton. The aqueous solution was extracted (10 hr.) with chloroform in a liquid–liquid extractor. Working up as above gave ricinine in 1·1% yield.

Isolation by Weever's procedure,[10] in which organic acids are removed as lead salts before extraction of the alkaloid, afforded ricinine in 0·9% yield. Tuson's even more cumbersome method [1] did not increase the yield.

Radioactivity Measurements.—A solution of pure ricinine (10 mg.) in a minimal volume of ethanol was evaporated by means of an infrared lamp on the surface of an aluminium disc (4·5 sq. cm.), slowly revolving on a turn-table. The radioactivity was measured by means of a Geiger–Müller end-window tube connected to a decimal counter (Ekco Electronics Ltd., Scaler type N 529A). The sample was placed in a lead castle 1 cm. from the tube window. Two tubes were used throughout this work: (*a*) Tracerlab, Inc. (end window) type TGC2, mica window, 1·8 mg./sq. cm.; (*b*) Nuclear Chicago (end window) type D34, mica window, 1·4 mg./sq. cm.

Table 1 summarises the results obtained with ricinine produced after feeding with DL-[2-^{14}C]-lysine hydrochloride.

[10] Cf. Weevers, *Rec. Trav. botan. Neerland*, 1932, **30**, 336.

XUM

TABLE 1.

Lysine hydrochloride		Ricinine		
Wt. (mg.)	Activity (μc)	Wt. (mg.)	Activity (10^3 c.p.m./millimole)	Tube
10	18·2	5	2·3	TGC 2
42·2	76·3	11	4·0	TGC 2
81·7	286·6	21	6·1	D34
74·2	261	25	54	D34
60	210	25	25	D34

Ozonisation of 4-Methoxy-1-methyl-2-pyridone.—The pyridone (II) (42 mg.) was suspended in dry ethyl acetate (2·5 ml.), and dry ozone (0·91 vol. %; large excess) was bubbled through the suspension at −60° from a Welsbach ozonator (model T-23) during 6 hr. The ozonisation flask was attached to a trap containing carbonate-free sodium hydroxide to absorb any carbon dioxide formed. The mixture was then oxidatively decomposed by the addition of 30% hydrogen peroxide (" AnalaR "; 2 ml.) with stirring at room temperature during 12 hr. without disconnexion of the carbon dioxide absorption tube. The solvents were then removed in a vacuum-desiccator over phosphorus pentoxide.

After attempted paper-chromatographic separation of the products, the following procedure, for which we are indebted to Dr. J. Avidor of the Israeli Institute of Biological Research, Ness Ziona, effected their separation: A portion of the solid residue after ozonisation (up to 30 mg.) was dissolved in dry ethanol (1 ml.). To this solution were added ether (2 ml.) and a solution (1·5 ml.) made up of equal volumes of 5% methanolic hydroxylamine hydrochloride and 12·5% methanolic sodium hydroxide. The mixture was kept at room temperature for 1 hr. and was neutralised with a few drops of acetic acid. It was then quantitatively transferred to sheets (25 × 25 cm.) of Whatman No. 3MM paper. Butanol–acetic acid–water (4 : 1 : 5) was run for 20 hr., the paper was dried at room temperature, and strips were sprayed either with a solution of ferric chloride in butanol [brown spot corresponding to the hydroxylamide (V)] or with Ferron solution [red spot corresponding to the amide (IV) which does not give a hydroxy-amide under the conditions described above].

Products (IV) and (V) were eluted from the paper by means of 75% ethanol in 85% and 65% yield, respectively.

An authentic specimen of the amide (IV) was prepared by the published procedure.[11] Potassium methyl oxalate [12] (12 mg.) was dissolved in ethanol (2 ml.) and ether (4 ml.) was added, then hydroxylamine hydrochloride. Working up and chromatography as described above and elution with 75% ethanol gave the hydroxy-amide.

The synthetic amide (IV) and hydroxy-amide (V) were identical in infrared spectra with the corresponding ozonolysis products.

Isolation of Carbon Dioxide from Ozonolysis.—The carbon dioxide absorbed in the trap attached was converted into barium carbonate.[13] Table 2 summarises the results of the radioactivity measurements made in a typical experiment, starting with labelled lysine hydrochloride (210 μc).

TABLE 2.

Compound	Activity (c.p.m./millimole)	Compound	Activity (c.p.m./millimole)
Ricinine (I)	$2·95 \times 10^3$	Acid amide (IV)	5
4-Methoxy-1-methyl-2-pyridone (II)	$9·8 \times 10^2$	Barium carbonate ($\equiv C_{(a)}$)	$6·08 \times 10^3$
Hydroxy-amide (V)	8		

Determination of Radioactivity in the Cyano-group.—(*a*) The published procedure was used.[3] Ricinine (20 mg.; $5·4 \times 10^3$ c.p.m./millimole) was heated with 57·4% sulphuric acid (1 ml.) at 140° for 1 hr., the resulting carbon dioxide being swept out with a stream of helium and absorbed in carbonate-free sodium hydroxide and then converted into barium carbonate (38·6 mg., 156% yield; $8·2 \times 10^2$ c.p.m./mmole). The mixture was neutralised (litmus) with sodium hydroxide

[11] Weddige, *J. prakt. Chem.*, 1902, **12**, 435.
[12] Skrabal, *Monatsh.*, 1917, **38**, 35.
[13] Hutchens, Claycomb, Cathey, and van Bruygen, *Nucleonics*, 1950, **7**, 41.

and extracted with chloroform. Drying the extract (Na_2SO_4) and removal of the solvent afforded colourless crystals (II) (11 mg., 65%), m. p. 113° (lit.,[3] m. p. 112—113°). (*b*) Labelled ricinine was converted into ricininic acid,[4] and the latter (20 mg.; $9{\cdot}2 \times 10^3$ c.p.m./millimole), suspended in water (0·7 ml.), was oxidised [4] with chromic acid (0·2 ml. of a solution of 200 mg. of chromium trioxide in 1 g. of concentrated sulphuric acid), whilst helium was passed through the mixture. Silver cyanide was precipitated, centrifuged, and dried at 105° to constant weight (17 mg., 97%; 19 c.p.m./millimole).

Determination of Radioactivity in OMe *and N-*Me *Groups.*—The published procedure was used.[5] We are indebted to Mr. E. Meier of the Weizmann Institute for Science of carrying out these determinations.

Ricinine (10 mg.; $2{\cdot}95 \times 10^3$ c.p.m./millimole) afforded tetramethylammonium reineckate from the methyl iodide corresponding to the methoxyl group (33 mg., 95% yield; 3·4 c.p.m./millimole) and to that corresponding to the *N*-methyl group (32·4 mg., 94% yield; 3·2 c.p.m./millimole).

Isolation of Amino-dicarboxylic Acids from Seedlings of Ricinus communis *L.*—Three-weeks-old etiolated seedlings (200 g.) were dried, powdered, extracted with ethanol, and worked up in the usual way.[14] Paper chromatography of the concentrated solution of amino-dicarboxylic acids [15] identified aspartic, glutamic, and α-aminoadipic acid. Two spots were not identified.

Isotopic Dilution Experiment with Nicotinic Acid.—Seedlings of *Ricinus communis* L. were grown as described above. In a control experiment feeding was carried out with DL-[2-^{14}C]-lysine hydrochloride (0·503%; 3 ml.; 100 μc) whilst in the parallel experiment the two-week-old seedlings were fed during 3 days with DL-[2-^{14}C]lysine hydrochloride (same amount) and nicotinic acid (1·91%; 6 ml.). After 3 additional days the seedlings were harvested and the alkaloid isolated in the usual way from each batch. The control gave ricinine (11·5 mg., $1{\cdot}84 \times 10^3$ c.p.m./millimole) whilst the nicotinic acid batch gave ricinine (17 mg.; $4{\cdot}5 \times 10^3$ c.p.m./millimole).

Labelled Ricinine from α-Amino[ε-^{14}*C]adipic Acid.*—The amino-acid (240 mg.; $1{\cdot}2 \times 10^6$ c.p.m./millimole) was prepared by the published procedure [6] in similar yield. It was fed to seedlings of *Ricinus communis* L. as described for the lysine-feeding experiments. Ricinine (15 mg.; $2{\cdot}6 \times 10^4$ c.p.m./millimole) was isolated in the usual way.

Determination of Radioactivity of the Cyano-group.—(*a*) Ricinine (11 mg.; $2{\cdot}6 \times 10^4$ c.p.m./millimole) was diluted with unlabelled ricinine (15 mg.) and hydrolysis of the cyano-group was effected by 57·4% sulphuric acid at 140° for 1 hr. Barium carbonate was isolated (77·5 mg.; 160%; $5{\cdot}3 \times 10^3$ c.p.m./millimole).

(*b*) Labelled ricinine (4 mg.; $2{\cdot}6 \times 10^4$ c.p.m./millimole) diluted with unlabelled ricinine (2 mg.) gave silver cyanide (3 mg.; 50 c.p.m./millimole).

Ozonisation of the Pyridone (II) *resulting from α-Amino*[ε-^{14}C]*adipic Acid.*—The pyridone was obtained in the usual way. Ozonisation of it (11·6 mg.; $2{\cdot}1 \times 10^4$ c.p.m./millimole) as described above afforded unlabelled hydroxy-amide (V) [corresponding to half-ester (III)], labelled carbon dioxide isolated as barium carbonate (9·3 mg.; $1{\cdot}09 \times 10^4$ c.p.m./millimole) and labelled amide (IV) (8 mg.; $0{\cdot}95 \times 10^4$ c.p.m./mmole).

Degradation of Labelled Amide (IV).—In a Schmidt reaction, a mixture of labelled amide (8 mg.; $0{\cdot}95 \times 10^4$ c.p.m./mmole) with unlabelled amide (IV) (4 mg.), sodium azide (23·5 mg.), and dry benzene (0·4 ml.) was treated with concentrated sulphuric acid (0·5 ml.) in two portions at room temperature. The flask was connected to a trap containing carbonate-free sodium hydroxide while helium was passed through the reaction mixture. The mixture was kept at 80° for 4 hr. Barium carbonate was prepared from the material in the trap in the usual way (24·2 mg., 103%; $1{\cdot}1 \times 10^2$ c.p.m./mmole).

To the cooled mixture attached to the trap was added 2N-sulphuric acid (0·4 ml.), helium was passed through the mixture, and the temperature was kept at 110° for 6 hr. Barium carbonate was isolated from the material in the trap (23 mg., 97%; $0{\cdot}9 \times 10^4$ c.p.m./mmole).

DEPARTMENT OF CHEMISTRY, ISRAEL INSTITUTE OF TECHNOLOGY,
HAIFA, ISRAEL. [*Received, March 16th,* 1959.]

[14] Pucher, Abrahams, and Vickery, *J. Biol. Chem.*, 1948, **172**, 579.
[15] Bergstrom and Paabo, *Acta Chem. Scand.*, 1949, **3**, 202.

XUM

586. *Cyclic Organic Boron Compounds. Part IV.*[1] B-*Amino-* and B-*Alkoxy-borazoles and their Precursors the Tris(primary amino)borons and (Primary amino)boron Alkoxides.*

By D. W. Aubrey and M. F. Lappert.

Interaction of boron trichloride with an excess of primary amine (R in $R{\cdot}NH_2$ = Me, Et, Pr^i, Bu^n, Bu^s, Bu^t, cyclohexyl, $Ph{\cdot}CH_2$, Ph) afforded the triaminoboron $B(NHR)_3$, which on pyrolysis afforded in the first instance the *B*-aminoborazole (I) and eventually the thermally stable (at least up to 600°) polymeric borazole (III). Similarly, the n-butoxyboron chlorides and ethylamine gave the primary aminoboron n-butoxides, which when heated gave the *B*-n-butoxyborazole (IV). The characterising constants and molecular weights of all the non-polymeric compounds have been determined.

The preparation of trisethylaminoboron, $(Et{\cdot}NH)_3B$, n-butyl bisethylaminoborinate, $Bu^nO{\cdot}B(NHEt)_2$, and di-n-butyl ethylaminoboronate, $(Bu^nO)_2B{\cdot}NHEt$, has been briefly described;[1] pyrolysis of the triaminoboron gave the borazole (I; R = Et) and eventually polyborazoles, whereas the n-butoxy-compounds gave the borazole (IV). These experiments are now described in detail and also reported are extensions to other monoalkylamino-, benzylamino-, and anilino-systems.

Addition of boron trichloride to a primary amine in an inert solvent at −78° afforded the triaminoboron in high yield (Table 1): $BCl_3 + 6R{\cdot}NH_2 \longrightarrow B(NHR)_3 + 3R{\cdot}NH_2,HCl$. The trisethylaminoboron,[1] and the phenyl,[2] *p*-tolyl,[3] and *p*-methoxyphenyl [4] compounds

Table 1. *Characterisation and yields of the triaminoborons,* $B(NHR)_3$.

R	Yield (%)	B. p./mm. (m. p.)	d_4^{20}	n_D^{20}	Molar refractivity Found	Calc.*
Me	71	59°/33	0·8871	1·4465	30·3	30·2
Et	55	62—63°/10	0·833	1·4380	44·9	44·8
Pr^i	81	37°/1	0·8000	1·4267	59·3	58·8
Bu^n	91	84°/0·005	0·8347	1·4462	72·4	72·6
Bu^s	92	49°/0·1	0·8186	1·4355	72·3	72·1
Bu^t	84	42°/0·05	0·7971	1·4272	72·8	73·4
Cyclohexyl	90	(92—94°)	—	—	—	—
$Ph{\cdot}CH_2$	80	Decomp.	1·0479	1·5805	104·8	103·9
Ph	81	Decomp.	—	—	—	—

* Based on Vogel's values ("A Text-book of Practical Organic Chemistry," Longmans, Green & Co., London, 1948, p. 900) and the value 3·0 for boron.

were the only previously described tris(primary amino)borons. The method hitherto used [2,3,4] for obtaining these trisarylaminoborons was more laborious than the present one and involved initial preparation of the amine–boron trichloride complex, and treatment of this with more amine under somewhat forcing conditions. In view of the eliminations which the tris-compounds undergo when heated (see below), mild reaction conditions for their preparation are preferable. Reference has been made to trisethylaminoboron (obtained from boron trifluoride, ethylamine, and lithium), but it was not characterised.[5]

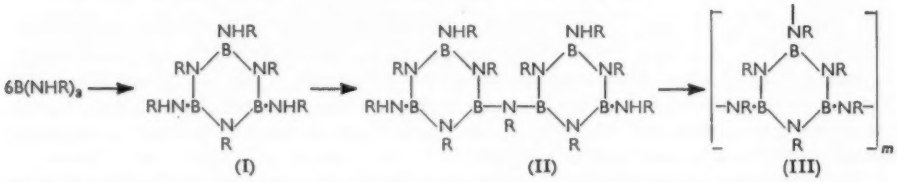
The characterising constants of the triaminoborons are shown in Table 1, as are the molar refractivities of the liquid members. Assigning a value of 3·0 for the atomic refractivity of boron gives fair agreement between experimental and calculated values for molar refractivities; the value in trialkyl borates is 2·65.[6] The compounds are monomeric (Table 3) and colourless liquids or crystals and are easily hydrolysed by cold water to the

[1] Lappert, *Proc. Chem. Soc.*, 1959, 59.
[2] Jones and Kinney, *J. Amer. Chem. Soc.*, 1939, **61**, 1378.
[3] Kinney and Kolbezen, *ibid.*, 1942, **64**, 1584.
[4] Kinney and Mahoney, *J. Org. Chem.*, 1943, **8**, 526.
[5] Kraus and Brown, *J. Amer. Chem. Soc.*, 1930, **52**, 4414.
[6] Lappert, *J.*, 1956, 1768.

primary amine and boric acid. The aliphatic compounds are soluble in non-polar solvents, such as pentane and benzene, but the benzyl compound was only sparingly soluble in pentane; the trianilinoboron was insoluble in pentane but soluble in hot benzene and chloroform.

Interaction of ethylamine and the n-butoxyboron chlorides afforded the ethylaminoboron n-butoxides: $(Bu^nO)_xBCl_{3-x} + 2(3-x)Et{\cdot}NH_2 \longrightarrow (Bu^nO)_xB(NHEt)_{3-x} + (3-x)Et{\cdot}NH_2{,}HCl$ ($x = 1$ or 2). These compounds are the first (primary amino)boron alkoxides to be reported, but four (secondary amino)boron alkoxides, $(Bu^nO)_xB(NR_2)_{3-x}$, are known.[7,8]

At 200° trisethylaminoboron was almost quantitatively converted in 3½ hr. into the borazole (I; R = Et). Further heating resulted in elimination of ethylamine, corresponding to formation of the condensation dimer (II), which ultimately at 600° afforded a polymer (III). Spectroscopic evidence (to be detailed later) has been outlined [1]



to show that compound (I) is a borazole and that compounds (II) and (III) are polyborazoles. The borazole (I; R = Et) was a viscous, colourless liquid, which during pyrolysis gradually darkened, increased in viscosity, changed to a light brown rubber (mobile liquid when hot), and finally into a dark brown, non-thermoplastic brittle resin, which was insoluble in inert organic solvents and was evidently highly cross-linked. The ultimate polymer was only slowly attacked by cold water, but was hydrolysed in boiling water to boric acid and ethylamine. A polymeric borazole, obtained as a distillation residue by redistilling the borazole (I; R = Et), was elastomeric, insoluble in organic solvents, and unaffected by boiling water, but hydrolysed by concentrated hydrochloric acid.

Other borazoles (Table 2) were obtained similarly, either as higher-boiling fractions obtained when distilling the triaminoborons, or as pyrolysis products (R = cyclohexyl, $Ph{\cdot}CH_2$, or Ph). Their molecular weights (Table 5) corresponded to formula (I), *i.e.*,

TABLE 2. *Characterisation of the* B-*aminoborazoles* (I).

R	B. p./mm. (m. p.)	d_4^{20}	n_D^{20}	Molar refractivity Found	Calc.*
Me	110°/0·1	1·016	1·5082	61·7	61·9
Et	145—150°/0·1	0·933	1·4826	89·8	89·8
Pr^i	106°/0·03	0·8220	1·4628	118·0	117·9
Bu^n	158°/0·005	0·900	1·4730	144·3	145·7
Bu^s	135°/0·01	0·892	1·4695	144·2	144·6
Bu^t	103°/0·04	0·883	1·4631	144·0	147·1
Cyclohexyl	(52—55°)	—	—	—	—
$Ph{\cdot}CH_2$	>250°/0·005	1·156	1·642	208·1	209·1
Ph	(152—155°)	—	—	—	—

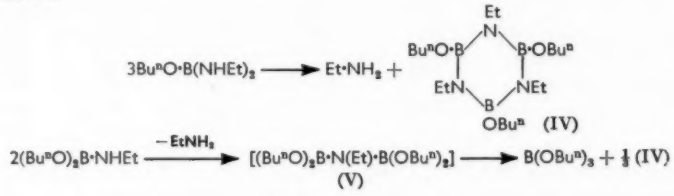
* See footnote to Table 1.

$(R{\cdot}NH{\cdot}B{\cdot}NR)_3$. When heated they polymerised further, except for the compound (I; R = Bu^t; this may be due to steric hindrance making elimination of t-butylamine difficult). The borazoles (I) were soluble in many non-polar organic solvents and, except for the phenyl compound, were easily hydrolysed by cold water; the phenylborazole was hydrolysed by hot water.

[7] Gerrard, Lappert, and Pearce, *J.*, 1957, 381.
[8] *Idem, Chem. and Ind.*, 1958, 292.

Preparation of *B*-aminoborazoles has previously (except for R = Et[1]) been described in only one other work,[9] the compounds then being obtained from *B*-chloroborazoles and amines. The polynuclear borazoles appear to be novel and are of interest because they are polymers having wholly inorganic skeletons, and because polycyclic inorganic compounds are virtually unknown. The remarkable thermal stability of the polymer (III; R = Et) is attributed to the absence of organic radicals in the main chain.

Pyrolysis of the ethylaminoboron n-butoxides afforded the borazole (IV); with di-n-butyl ethylaminoboronate there was no evidence for the presumed intermediate (V). The molecular weight and the infrared spectrum[1] of the intermediate were consistent with its formulation as a *B*-alkoxyborazole; such compounds were unknown before our earlier[1] communication.



Experimental

General Procedures.—Amines were dried and purified by heating under reflux with, and fractionation from, barium oxide. Analysis for chlorine was by Volhard's method, for boron by Thomas's method,[10] for nitrogen either as amino-group by steam distillation from potassium hydroxide and distillation into standard acid, or by the Kjeldahl procedure (for I; R = Ph). Molecular weights were determined ebullioscopically in benzene. The identity of the amines, obtained as pyrolysis products during formation of borazoles, was established by demonstrating their identity with authentic specimens by gas chromatography and infrared spectroscopy.

Preparation of Triaminoborons.—Boron trichloride (1 mol.; usually 0·1 mole) in n-pentane (25 c.c.) at −78° was added slowly from a cooling-jacketed dropping funnel to the amine (6 mol.) in n-pentane (250 c.c.) at −78°. Reaction was invariably highly exothermal and accompanied by formation of a white precipitate. The mixture was set aside for 2 hr. at 20° and then filtered. The precipitate which was exclusively the amine hydrochloride in all except the benzylamine and aniline experiments (when it was a mixture of the amine hydrochloride and triaminoboron) was washed with more solvent, freed from solvent at 20°/15 mm., weighed, and analysed; from the filtrate, after removal of solvent, there was obtained the crude triaminoboron which was purified by fractional distillation or crystallisation (the yields shown in Table 1 are of purified product). In the benzylamine and aniline experiments the components of the precipitate were separated by extracting the triaminoboron with hot benzene. Attempted

Table 3. *Analysis of the triaminoborons*, B(NHR)$_3$.

	Found					Required				
R	C (%)	H (%)	N (%)	B (%)	*M*	C (%)	H (%)	N (%)	B (%)	*M*
Me	35·6	11·5	41·0	11·2	106	35·7	11·9	41·7	10·7	101
Et	50·4	12·4	29·0	7·9	146	50·3	12·7	29·4	7·7	143
Pr^i	58·3	12·5	22·5	5·8	188	58·5	12·9	22·7	5·8	185
Bu^n	62·8	13·2	18·5	4·8	217	63·4	13·2	18·5	4·8	227
Bu^s	64·5	13·5	18·0	4·7	231	63·4	13·2	18·5	4·8	227
Bu^t	63·7	13·2	18·3	4·7	243	63·4	13·2	18·5	4·8	227
Cyclohexyl	71·3	12·2	13·9	3·8	302	70·8	11·8	13·9	3·5	305
Ph·CH$_2$	76·5	7·6	12·7	3·0	332	76·6	7·3	12·8	3·3	329
Ph			14·6	3·8				14·7	3·8	

distillation of trisbenzylaminoboron resulted in elimination of benzylamine, but the undistilled material was pure as shown by analysis and molecular-weight determination. The yields and characterisation of the triaminoborons are shown in Table 1, whilst in Tables 3 and 4 are shown the analytical data for the triaminoborons and the amine hydrochlorides respectively.

[9] Gould, U.S.P. 2,754,177/1956.
[10] Thomas, *J.*, 1946, 820.

Preparation of Borazoles (I).—Only for ethylamino- (83%), cyclohexylamino- (100%), benzylamino- (100%), and anilino-borazole (100%) do the stated yields have meaning, because in the remaining experiments no separate effort was made to pyrolyse appropriate triaminoborons, the corresponding borazoles [R in $(R{\cdot}NH{\cdot}B{\cdot}NR)_3$ = Me (4·3%), Pr^i (14·7%), Bu^n (15·8%), Bu^s (16·3%), Bu^t (18·4%)] being obtained merely as higher-boiling fractions during the preparation of the triaminoborons.

TABLE 4. *Yield and analysis of* $R{\cdot}NH_2$,HCl.

		Found (%):		Calc. (%):	
R	Yield (mols.)	N	Cl	N	Cl
Me	3·12	20·5	50·0	20·7	52·5
Et	3·02	17·3	43·3	17·2	43·6
Pr^i	2·68	14·5	37·0	14·7	37·1
Bu^n	2·98	12·6	31·9	12·8	32·4
Bu^s	3·03	13·1	32·4	12·8	32·4
Bu^t	2·89	12·6	29·5	12·8	32·4
Cyclohexyl	3·07	10·5	24·3	10·3	26·2
$Ph{\cdot}CH_2$	3·42	9·9	23·5	9·8	24·7
Ph	3·27	11·3	25·5	10·8	27·4

The triaminoborons were pyrolysed under reflux (R = Et at 200° for 3½ hr.; R = cyclohexyl at 200°/0·1 mm. for 5 hr.; R = $Ph{\cdot}CH_2$ at 250°/0·005 mm. for 2 hr.; R = Ph at 250°/10 mm. for 2 hr.), under conditions such that elimination of amine (collected as a condensate at −78°) corresponded to that required for borazole formation. The *B*-ethylaminoborazole was then distilled, but this was not possible for the others. Characterisation of the borazoles (I) is shown in Table 2, and in Table 5 are the analytical data.

TABLE 5. *Analysis of the* B-*aminoborazoles* (I).

	Found					Required				
R	C (%)	H (%)	N (%)	B (%)	*M*	C (%)	H (%)	N (%)	B (%)	*M*
Me	33·4	9·8	40·0	15·7	211	34·3	10·1	40·1	15·5	210
Et	48·5	11·0	28·8	11·1	290	49·0	11·2	28·6	11·3	294
Pr^i	56·1	11·5	22·4	8·9	365	57·2	12·0	22·2	8·6	378
Bu^n	62·0	12·4	18·1	7·3	446	62·3	12·4	18·2	7·0	462
Bu^s	61·8	12·1	18·0	7·2	471	62·3	12·4	18·2	7·0	462
Bu^t	61·5	12·0	18·3	7·2	445	62·3	12·4	18·2	7·0	462
Cyclohexyl *	71·3	10·8	13·4	4·9	564	69·9	11·3	13·8	5·3	618
$Ph{\cdot}CH_2$ *	73·4	6·6	12·4	5·2	579	75·6	6·8	12·6	4·9	666
Ph *	72·1	5·8	13·6	5·8	541	74·2	5·7	14·4	5·6	582

* Undistilled.

Pyrolysis of the Borazole (I; R = Et).—The borazole (11·40 g.) was not appreciably changed at 200° in 3 hr. At 300°, however, ethylamine [0·87 g. Calc., 0·86 g., for formation of (II)] was eliminated during 4 hr. and further heating at 300° had little effect. At 320° evolution of ethylamine continued and after 5 hr. the amount corresponded approximately to the formation of the linear decacyclic borazole. A total of 1·65 g. of ethylamine had been evolved and a further loss in weight of 2·36 g. occurred after 9 hr. at ~600° to leave the polymer, a section of which is formulated as (III).

Interaction of Butyl Dichloroborinate and Ethylamine.—The dichloroborinate [11,12] (10·30 g., 1 mol.) in n-pentane (20 c.c.) was slowly added to the amine (14·03 g., >4 mol.) in n-pentane (30 c.c.) at −78°. The reaction was highly exothermal. The precipitated ethylamine hydrochloride (10·53 g., 97%) (Found: N, 17·0; Cl, 43·5%) was filtered off and the residue obtained from the filtrate by evaporation was fractionated, to give (i) 4·07 g., b. p. 37—38°/0·2 mm., n_D^{20} 1·4223, d_4^{20} 0·826 (Found: N, 12·7; B, 6·9%), (ii) 2·94 g., b. p. 38—39°/0·2 mm., n_D^{20} 1·4200, (iii) crude borazole (IV), 3·13 g., b. p. 128—129°/0·1 mm., n_D^{20} 1·4595, d_4^{20} 0·935 (Found: N, 11·7; B, 9·0%), and a residue (0·84 g.). There was no condensate. Components (i) and (ii) were combined and after three successive fractionations, there was obtained *n-butyl bisethylaminoborinate* (3·13 g., 28%) (Found: C, 55·4; H, 12·2; N, 16·0; B, 6·2%; *M*, 180.

[11] Gerrard and Lappert, *J.*, 1951, 2545.
[12] *Idem*, *J.*, 1955, 3084.

$C_8H_{21}ON_2B$ requires C, 55·8; H, 12·3; N, 16·3; B, 6·3%; *M*, 172), b. p. 38—39°/0·2 mm., n_D^{20} 1·4280, d_4^{20} 0·839. Examination of the other fractions indicated that some disproportionation, as well as elimination of amine to give the borazole (IV) [2·32 g., obtained from (iii), b. p. 152—154°/0·3 mm., n_D^{20} 1·4540 (Found: N, 10·9; B, 8·5%)], had also taken place.

Interaction of Di-n-butyl Chloroboronate and Ethylamine.—By a similar procedure there was obtained from the chloroboronate[6,11] (27·8 g., 1 mol.) and the amine (16·00 g., >2 mol.) in n-pentane (total 100 c.c.), ethylamine hydrochloride (11·50 g., 98%) (Found: N, 17·1; Cl, 43·5%) as insoluble product. The filtrate, after several redistillations, afforded *di-n-butyl ethylaminoboronate* (8·23 g., 28%), b. p. 49—51°/0·1 mm., n_D^{20} 1·4178, d_4^{20} 0·846 (Found: C, 59·9; H, 12·3; N, 7·4; B, 5·6%; *M*, 211. $C_{10}H_{24}O_2NB$ requires C, 59·7; H, 12·0; N, 7·6; B, 5·4%; *M*, 201). Analyses and physical constants of other fractions indicated that disproportionation of the aminoboronate (to give the triaminoboron, the diaminoborinate, and the borate) also occurred; only a trace of (IV) was isolated.

Pyrolysis of the Ethylaminoboron n-Butoxides.—n-Butyl bisethylaminoborinate (4·17 g.) was heated under reflux. After 1 hr. at 160° no ethylamine had been lost, but at 260° (2½ hr.) the amine (0·84 g., 77%) (characterised by gas chromatography) was collected as a condensate. The residue, after two distillations, afforded the borazole (IV) (2·06 g., 66%), b. p. 153—156°/0·4 mm., n_D^{20} 1·4544, d_4^{20} 0·935 (Found: C, 56·0; H, 12·1; N, 11·0; B, 8·6%; *M*, 394. $C_{18}H_{42}O_3N_3B_3$ requires C, 56·7; H, 11·0; N, 11·0; B, 8·6%; *M*, 381).

Similarly, from di-n-butyl ethylaminoboronate (13·85 g.) there were obtained (after 5½ hr. at 220°) ethylamine (1·24 g., 80%), tri-n-butyl borate (6·92 g., 87%), b. p. 48—52°/0·2 mm., n_D^{20} 1·4100 (authentic infrared spectrum), and the borazole (IV) (2·44 g., 56%), b. p. 153—157°/0·4 mm., n_D^{20} 1·4530 (Found: N, 10·8; B, 8·5%). The pyrolysis mixture before distillation was shown (infrared spectrum) to be a mixture of the borate and borazole.

We thank Mr. H. Pyszora for the infrared spectral measurements made at the National College of Rubber Technology (Northern Polytechnic), and Dr. W. Gerrard for his continued encouragement.

NORTHERN POLYTECHNIC, HOLLOWAY ROAD, LONDON, N.7. [*Received, April 3rd*, 1959.]
[*Present Address* (M. F. L.).—MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY].

---

587. *Metallic Complexes of Dimethyl-o-methylthiophenylarsine. Part II.*[1] *Complexes of Copper, Silver, and Gold.*

By B. CHISWELL and S. E. LIVINGSTONE.

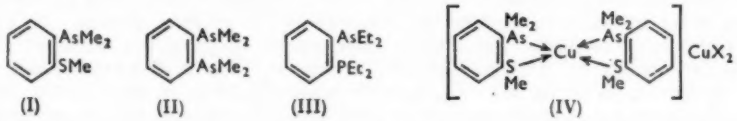
The complexes formed by univalent copper, silver, and gold with dimethyl-*o*-methylthiophenylarsine (As–S) are described. Copper forms soluble complexes of two types: (*a*) Cu(As–S)X (X = Cl, Br, I) and (*b*) $Cu(As–S)_2X$ (X = Cl, Br, I, ClO_4); an insoluble complex, Cu(As–S)SCN, was also isolated. Silver forms insoluble complexes, $Ag(As–S)_2X$ (X = Cl, Br, I). Gold forms soluble complexes of two types: (i) Au(As–S)X (X = Cl, Br, I) and (ii) $Au(As–S)_3ClO_4$.

COMPLEXES of bivalent nickel and palladium with the chelate compound, dimethyl-*o*-methylthiophenylarsine (I), have been described.[1] This paper reports the complexes formed by univalent copper, silver, and gold with this ligand. It is of interest to compare these complexes with those of *o*-phenylenebisdimethylarsine (II) with copper [2] and gold,[3] and those of *o*-diethylphosphinophenyldiethylarsine (III) with copper, silver, and gold.[4]

With the arsine (I) copper forms colourless complexes which are of two types: (*a*) Cu(As–S)X (As–S = dimethyl-*o*-methylthiophenylarsine; X = Cl, Br, I, SCN), and (*b*) $Cu(As–S)_2X$ (X = Cl, Br, I, ClO_4). The former were prepared by treating an aqueous

[1] Livingstone, *Chem. and Ind.*, 1957, 143; Part I, *J.*, 1958, 4222.
[2] Kabesh and Nyholm, *J.*, 1951, 38.
[3] Harris and Nyholm, *J.*, 1957, 63.
[4] Cochran, Hart, and Mann, *J.*, 1957, 2816.

solution of cuprous halide in an excess of the corresponding potassium halide with an alcoholic solution of the arsine (I). The compounds $Cu(As{-}S)_2X$ (X = Cl, Br, I) can be obtained if an excess of arsine is added to the cuprous halide solution and the mixture is heated under reflux. The perchlorate, $Cu(As{-}S)_2ClO_4$, is precipitated when an aqueous



(I) (II) (III) (IV)

solution of copper sulphate containing perchloric acid is treated with an alcoholic solution of the arsine (I). The cuprous compounds which were prepared and their conductivities in nitrobenzene are listed in Table 1.

TABLE 1. *Molecular conductivities of cuprous complexes of dimethyl-o-methylthiophenylarsine.*

Compounds	Concn. (10^{-3}M)	Mol. condy. in $Ph{\cdot}NO_2$ at 25° (mho)	Compounds	Concn. (10^{-3}M)	Mol. condy. in $Ph{\cdot}NO_2$ at 25° (mho)
$[Cu(As{-}S)_2][CuCl_2]$	1·00	22·2	$[Cu(As{-}S)_2]ClO_4$	1·64	26·2
$[Cu(As{-}S)_2][CuBr_2]$ ...	1·08	25·8	$[Cu(As{-}S)_2]Cl$ ...	1·31	14·1
$[Cu(As{-}S)_2][CuI_2]$	2·04	30·4	$[Cu(As{-}S)_2]Br$ ...	1·46	10·4
$[Cu(As{-}S)_2][Cu(SCN)_2]$	Insol. in $Ph{\cdot}NO_2$	—	$[Cu(As{-}S)_2]I$ ...	2·08	4·1

Conductivity measurements in nitrobenzene solution show that the compounds $Cu(As{-}S)X$ (X = Cl, Br, I) are uni-univalent electrolytes and that their formulæ should be doubled, *viz.*, $[Cu(As{-}S)_2][CuX_2]$. If the arsine (I) is acting as a chelate group, which seems most likely, the copper atom in the cation is quadricovalent and probably tetrahedral. The compounds would then have the structure (IV). The dithiocyanatocuprate(I) complex is insoluble in nitrobenzene, alcohol, and water. This insolubility suggests that its structure may differ from that of the halogenocuprate(I) complexes $[Cu(As{-}S)]_2[CuX_2]$. Consequently, the infrared absorption spectrum of the compound was obtained in order to ascertain whether the compound has a polymeric structure in which the thiocyanato-groups are bridging. For a number of thiocyanato-complexes of bivalent palladium and platinum it has been shown [5] that those complexes which contain bridging –SCN groups display an absorption maximum at 2154—2182 cm.$^{-1}$, while those in which the –SCN group is terminal have maxima in the range 2105—2120 cm.$^{-1}$. Silver thiocyanate, which contains bridging –SCN groups,[6] has a maximum [7] at 2149 cm.$^{-1}$. The thiocyanato-complex with the arsine (I) displays a maximum at 2103 cm.$^{-1}$, suggesting that the –SCN group is terminal and not bridging. The infrared absorption spectra of some other compounds which contain terminal –SCN groups were examined in this region and the maxima are listed in Table 2.

TABLE 2. *Thiocyanate stretching frequencies* (cm.$^{-1}$).

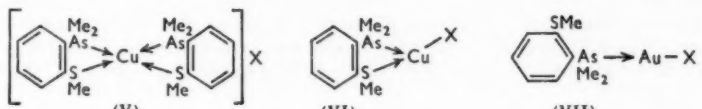
$Cu(As{-}S)(SCN)$	2103	$K_2[Pt(SCN)_4]$	2116
$[Pd(As{-}S)(SCN)_2]$	2094	$K_2[Pt(SCN)_6]$	2118
$K_2[Pd(SCN)_4]$	2115, 2090		

The perchlorate, $Cu(As{-}S)_2ClO_4$, behaves as a uni-univalent electrolyte in nitrobenzene and possesses the same cation, $[Cu(As{-}S)_2]^+$, as the halogenocuprate(I) complexes. In nitrobenzene solution the compounds $Cu(As{-}S)_2X$ (X = Cl, Br, I) have conductivities

[5] Chatt and Duncanson, *Nature*, 1956, **178**, 997.
[6] Lindqvist, *Acta Cryst.*, 1957, **10**, 29.
[7] Chatt, Duncanson, Hart, and Owston, *Nature*, 1958, **181**, 43.

XUM

which decrease in the order Cl > Br > I and are less than that expected for uni-univalent electrolytes (20—30 mho). A molecular-weight determination for the iodo-complex gave the value 284 (theor., 646). This result precludes any dimeric bridged structure. A tentative suggestion is that the compounds exist in the ionic form (V) in the solid state, but in nitrobenzene solution there is an equilibrium between the ionic form (V) and the structure



(V) (VI) (VII)

(VI), where one molecule of ligand has split off. The structure (VI) does not necessarily imply tercovalent copper since the fourth co-ordination position could be occupied by a molecule of solvent. This splitting off of the chelate group, dimethyl-*o*-methylthiophenylarsine, in nitrobenzene solution is known to occur with palladium complexes containing two molecules of this ligand.[1] An iodo-complex of silver with *o*-diethylphosphinophenyldiethylarsine (III) has been postulated by Cochran, Hart, and Mann [4] as existing in nitrobenzene and chloroform solutions partly in a form with a structure analogous to (VI).

With copper dimethyl-*o*-methylthiophenylarsine behaves similarly to *o*-phenylenebisdimethylarsine (As–As) and *o*-diethylphosphinophenyldiethylarsine (As–P). The last two chelate groups form complexes $[Cu(As–As)_2]Y$ (Y = Br, I, ClO_4, $CuCl_2$, $CuBr_2$, CuI_2) and $[Cu(As–P)_2]Z$ (Z = Cl, Br, I, $CuCl_2$, $CuBr_2$), respectively.

The silver complexes which were isolated in this investigation have the general formula $Ag(As–S)_2X$ (X = Cl, Br, I). They were prepared by treating a solution of the silver halide in aqueous potassium halide with an alcoholic solution of the arsine (I). All are insoluble in water and organic solvents. When warmed with alcohol, benzene, or nitrobenzene the complexes decompose, leaving a residue of silver halide. Their insolubility makes it unlikely that they are salts of the type $[Ag(As–S)_2]X$ or $[Ag(As–S)_4][AgX_2]$ since *o*-diethylphosphinophenyldiethylarsine (III) forms soluble complexes of general formula $[Ag(As–P)_2]Y$ (Y = I, $AgCl_2$, AgI_2).[4] With diphenylmethylarsine silver iodide forms a complex, $Ag(AsPh_2Me)_2I$, which is also insoluble in water and organic solvents and is decomposed on being warmed with alcohol or benzene. These complexes differ from those formed by silver iodide with certain other tertiary arsines AsR_3 (R = Et, Pr^n). These compounds AsR_3,AgI are readily soluble in organic solvents and are tetrameric in solution and in the solid state.[8] The insolubility of the silver halide complexes of dimethyl-*o*-methylthiophenylarsine suggests that they have a polymeric structure, but otherwise their structure is unknown.

The reaction of sodium tetrachloroaurate(III) with dimethyl-*o*-methylthiophenylarsine in alcohol, containing hypophosphorous acid, gives a colourless solution. The addition of halide ions causes deposition of aurous complexes, which can be recrystallised from alcohol and have the general formula Au(As–S)X (X = Cl, Br, I). Treatment of the above solution with perchloric acid precipitates a perchlorate, $Au(As–S)_3ClO_4$. The halogeno-complexes are non-electrolytes in nitrobenzene solution, while the perchlorate is a uni-univalent electrolyte in this solvent. The iodo-complex, Au(As–S)I, is monomeric in freezing nitrobenzene. It is probable that in the halogeno-complexes the ligand is unidentate (structure VII) and the gold atom has a covalency of two. Nothing definite can be said about the structure of the perchlorate, $Au(As–S)_3ClO_4$.

While the cuprous complexes of dimethyl-*o*-methylthiophenylarsine are similar to those of the diarsine (II) and the phosphine-arsine (III), the aurous complexes differ from those of these ligands, and the argentous complexes from those formed by (III).

[8] Mann, Wells, and Purdie, *J.*, 1937, 1828.

Experimental

Bisdimethyl-o-methylthiophenylarsinecopper(I) *Dichlorocuprate*(I).—Freshly prepared cuprous chloride (2 g.) was dissolved in saturated aqueous potassium chloride solution (30 ml.) containing concentrated hydrochloric acid (1 drop), and the solution was filtered. To the filtrate was added dimethyl-*o*-methylthiophenylarsine (1·5 g.) dissolved in alcohol (90 ml.). A precipitate, which was at first oily, was formed. The mixture was evaporated to half its volume, cooled, and filtered. The crystalline product was washed with hot water, then alcohol, and recrystallised from alcohol. The white crystals of the *compound* (0·6 g.) were dried over phosphorus pentoxide (Found: C, 32·5; H, 3·8; Cl, 10·4; Cu, 19·8. $C_{18}H_{26}Cl_2S_2As_2Cu_2$ requires C, 33·0; H, 4·0; Cl, 10·8; Cu, 19·4%).

Bisdimethyl-o-methylthiophenylarsinecopper(I) *Dibromocuprate*(I).—Dimethyl-*o*-methylthiophenylarsine (1·5 g.) in alcohol (90 ml.) was added to the solution obtained by dissolving cuprous bromide (1 g.) in saturated aqueous potassium bromide solution (30 ml.) containing concentrated hydrobromic acid (1 drop). The resultant oily precipitate was rendered crystalline by boiling and concentration of the solution to remove most of the alcohol. The solution was cooled and the white crystalline *product* was filtered off, washed with saturated potassium bromide solution, then with water, and finally with a small amount of alcohol (yield, 0·7 g.) (Found: C, 29·0; H, 3·4; Br, 21·5; Cu, 17·1. $C_{18}H_{26}Br_2S_2As_2Cu_2$ requires C, 29·1; H, 3·5; Br, 21·5; Cu, 17·1%).

Bisdimethyl-o-methylthiophenylarsinecopper(I) *Di-iodocuprate*(I).—Dimethyl-*o*-methylthiophenylarsine (1·2 g.) in alcohol (20 ml.) was added to a solution of cuprous iodide (2 g.) in saturated aqueous potassium iodide (20 ml.). The white crystalline product was filtered off and washed well with water. Recrystallisation from alcohol gave the pure *compound* as a white powder (1·4 g.) (Found: C, 25·7; H, 3·1; I, 30·4; Cu, 14·9. $C_{18}H_{26}I_2S_2As_2Cu_2$ requires C, 25·8; H, 3·1; I, 30·3; Cu, 15·2%).

Bisdimethyl-o-methylthiophenylarsinecopper(I) *Dithiocyanatocuprate*(I).—Freshly prepared cuprous chloride was dissolved in a saturated aqueous solution (50 ml.) of potassium thiocyanate. The solution was filtered and then treated with an alcoholic solution (50 ml.) of dimethyl-*o*-methylthiophenylarsine (1·5 g.). The *compound* was precipitated as a white powder, which was filtered off, and washed with water, then alcohol (yield, 1·5 g.) (Found: C, 34·3; H, 3·9; N, 4·0; Cu, 17·9. $C_{20}H_{26}N_2S_4As_2Cu_2$ requires C, 34·4; H, 3·7; N, 4·0; Cu, 18·2%).

Bisdimethyl-o-methylthiophenylarsinecopper(I) *Perchlorate*.—Copper sulphate pentahydrate (0·65 g.) was dissolved in water (20 ml.) containing 70% perchloric acid (5 ml.). To the filtered solution was added an alcoholic solution (40 ml.) of dimethyl-*o*-methylthiophenylarsine (1·5 g.). The mixture was shaken for 5 min. and the white crystalline *perchlorate* separated. It was filtered off, washed with water, then alcohol, and dried over phosphorus pentoxide (yield, 1·2 g.) (Found: C, 35·1; H, 4·1; Cu, 10·3. $C_{18}H_{26}O_4ClS_2As_2Cu$ requires C, 34·9; H, 4·2; Cu, 10·3%).

Bisdimethyl-o-methylthiophenylarsinecopper(I) *Chloride*.—Cuprous chloride (0·12 g.), dissolved in saturated aqueous potassium chloride solution (15 ml.), was mixed with dimethyl-*o*-methylthiophenylarsine (0·5 g.) in alcohol (50 ml.) and the mixture was heated under reflux for 2 hr. Water (20 ml.) was then added and the solution was evaporated to 30 ml. On cooling, the solution deposited white crystals, which were filtered off and washed with water. The product was dissolved in alcohol (10 ml.) and reprecipitated by the addition of water (50 ml.). The precipitate was filtered off, washed with water, followed by a little alcohol, and dried *in vacuo* (P_2O_5), yielding the *copper chloride complex* (0·3 g.) (Found: C, 38·1; H, 4·5; Cl, 6·4; Cu, 11·7. $C_{18}H_{26}ClS_2As_2Cu$ requires C, 38·9; H, 4·7; Cl, 6·4; Cu, 11·5%).

Bisdimethyl-o-methylthiophenylarsinecopper(I) *Bromide*.—Cuprous bromide (0·15 g.), dissolved in saturated aqueous potassium bromide solution (15 ml.), was mixed with dimethyl-*o*-methylthiophenylarsine (0·5 g.) in alcohol (50 ml.). Treatment as in the previous case, finishing with washing with saturated aqueous potassium bromide solution, then water, and recrystalisation twice from 50% alcohol, gave the white *bromide* (0·2 g.) (Found: C, 37·0; H, 4·4; Br, 13·0; Cu, 10·4. $C_{18}H_{26}BrS_2As_2Cu$ requires C, 36·0; H, 4·4; Br, 13·3; Cu, 10·6%).

Bisdimethyl-o-methylthiophenylarsinecopper(I) *Iodide*.—Cuprous iodide (0·2 g.), in saturated potassium iodide solution (15 ml.), and the arsine (0·5 g.) in alcohol (50 ml.), similarly gave an oil which became crystalline overnight. It was filtered off, washed with saturated potassium iodide solution, then with water, and recrystallised from 50% alcohol and dried (P_2O_5) to give the white *iodide* (0·3 g.) (Found: C, 33·1; H, 3·8; I, 19·2; Cu, 9·5%; *M*, cryoscopically in

XUM

0·91% nitrobenzene solution, 284. $C_{18}H_{26}IS_2As_2Cu$ requires C, 33·4; H, 4·1; I, 19·6; Cu, 9·8%; *M*, 646).

Iodobisdimethyl-o-methylthiophenylarsinesilver(I).—Freshly prepared silver iodide (1·5 g.) was dissolved in saturated potassium iodide solution (50 ml.); a solution of dimethyl-*o*-methylthiophenylarsine (1·5 g.) in alcohol (50 ml.) was added, and the mixture was vigorously shaken for 15 min. and kept for 2 hr. The resulting white precipitate was filtered off, washed with saturated potassium iodide solution, then several times with water, and finally with acetone, and dried over phosphoric oxide. The yield of *silver complex* was 1·5 g. (Found: C, 30·2; H, 3·5; I, 18·5; Ag, 15·8. $C_{18}H_{26}S_2As_2IAg$ requires C, 31·2; H, 3·8; I, 18·4; Ag, 15·6%). The compound is insoluble in water, alcohol, acetone, and nitrobenzene.

Bromobisdimethyl-o-methylthiophenylarsinesilver(I).—By a procedure similar to that used for the iodo-complex, silver bromide (1 g.), dimethyl-*o*-methylthiophenylarsine (1·2 g.), saturated potassium bromide solution (50 ml.), and alcohol (50 ml.) gave a precipitate, which was washed free from potassium bromide. The off-white precipitate was boiled with alcohol, filtered off, washed with alcohol, and dried, to give the *bromo-complex* (1·6 g.) (Found: C, 32·4; H, 3·7; Br, 12·5; Ag, 16·9. $C_{18}H_{26}BrS_2As_2Ag$ requires C, 33·6; H, 4·1; Br, 12·4; Ag, 16·8%).

Chlorobisdimethyl-o-methylthiophenylarsinesilver(I).—Freshly prepared silver chloride (0·7 g.), in saturated aqueous potassium chloride solution (50 ml.), was treated with an alcoholic solution (40 ml.) of dimethyl-*o*-methylthiophenylarsine (1·2 g.). The mixture was shaken for 30 min. while an oil separated. When washed with water the *product* became crystalline. It was then heated with alcohol and filtered off, washed with alcohol, and dried (P_2O_5) (yield, 1 g.) (Found: C, 35·7; H, 4·5; Cl, 6·1; Ag, 18·2. $C_{18}H_{26}ClS_2As_2Ag$ requires C, 36·0; H, 4·4; Cl, 5·9; Ag, 18·0%).

Iododimethyl-o-methylthiophenylarsinegold(I).—A solution of sodium tetrachloroaurate(III) (0·8 g.) in alcohol (10 ml.) was added with stirring to dimethyl-*o*-methylthiophenylarsine (1 g.) in alcohol (20 ml.) containing 30% hypophosphorous acid (4 ml.). On being heated the solution became colourless and deposited a small amount of reddish metallic gold. After filtration, the solution was treated with water (20 ml.), then heated to boiling, and sodium iodide (2 g.) in alcohol (30 ml.) was added. Upon cooling, the solution deposited a greyish-white product, which was recrystallised from alcohol to give the white, pure *compound* (0·8 g.) (Found: C, 19·5; H, 2·5; I, 23·1; Au, 35·8%; *M*, cryoscopically in 1·07% nitrobenzene solution, 569. $C_9H_{13}ISAsAu$ requires C, 19·6; H, 2·4; I, 23·0; Au, 35·7%; *M*, 552). The compound decomposes when heated. Its molecular conductance (Λ_{1000}) in nitrobenzene at 25° was 0·1 mho cm.$^{-2}$.

Bromodimethyl-o-methylthiophenylarsinegold(I).—The arsine (1 g.) and 30% hypophosphorous acid (4 ml.) in alcohol (40 ml.) were treated with sodium tetrachloroaurate(III) dihydrate (0·8 g.) in alcohol (10 ml.) as above and the mixture was boiled and filtered. The filtrate was diluted with water (20 ml.), treated with 34% hydrobromic acid, and kept 1 hr. The white crystalline *compound*, which was deposited, was filtered off and recrystallised from alcohol (yield, 1 g.) (Found: C, 21·6; H, 2·8; Br, 15·8; Au, 39·4. $C_9H_{13}BrSAsAu$ requires C, 21·4; H, 2·6; Br, 15·8; Au, 39·0%). The molecular conductance (Λ_{1000}) in nitrobenzene at 25° was 0·1 mho cm.$^{-2}$.

Chlorodimethyl-o-methylthiophenylarsinegold(I).—A solution of sodium tetrachloroaurate(III) dihydrate (0·4 g.) in alcohol (10 ml.) was added quickly, with stirring, to dimethyl-*o*-methylthiophenylarsine (0·5 g.) in alcohol (10 ml.). A white product started to crystallise after the addition was complete. After 2 hr. the crystalline *product* was filtered off, washed with water until free from sodium chloride, then with a small amount of alcohol, followed by ether, and dried (P_2O_5) (yield, 0·2 g.) (Found: C, 23·7; H, 2·6; Cl, 7·6; Au, 42·6. $C_9H_{13}ClSAsAu$ requires C, 23·5; H, 2·8; Cl, 7·7; Au, 42·8%). The molecular conductance (Λ_{1000}) in nitrobenzene at 25° was 0·1 mho cm.$^{-2}$.

Trisdimethyl-o-methylthiophenylarsinegold(I) *Perchlorate*.—A solution of sodium tetrachloroaurate(III) dihydrate (0·8 g.) in alcohol (10 ml.) was added with stirring to dimethyl-*o*-methylthiophenylarsine (1 g.) in alcohol (20 ml.) containing hypophosphorous acid (4 ml.). The solution was boiled, filtered, and treated with 60% perchloric acid (10 ml.). The resulting brownish precipitate was recrystallised twice from 50% aqueous alcohol to give the off-white *perchlorate* (Found: C, 33·0; H, 4·0; Au, 20·0. $C_{27}H_{39}O_4ClS_3As_3Au$ requires C, 33·0; H, 4·0; Au, 20·1%), Λ_{1000} in nitrobenzene at 25°, 28·6 mho cm.$^{-2}$.

Iodobisdiphenylmethylarsinesilver(I).—Diphenylmethylarsine (0·6 g.) in alcohol (10 ml.) was added to a solution of silver iodide (0·25 g.) in saturated aqueous potassium iodide (30 ml.).

The mixture was shaken for 5 min. and kept for 1 hr. The resulting white precipitate was filtered off, washed with saturated potassium iodide solution, followed by water, then alcohol, and dried, to yield the *compound* as a white powder (0·5 g.) (Found: C, 42·5; H, 3·4; I, 17·5; Ag, 14·9. $C_{26}H_{26}IAs_2Ag$ requires C, 43·2; H, 3·6; I, 17·5; Ag, 14·9%).

Infrared Spectra.—The spectra were obtained from Nujol mulls, sodium chloride optics being used.

Microanalyses for carbon, hydrogen, and nitrogen were carried out by Dr. E. Challen of the microanalytical laboratory of this university.

DEPARTMENT OF INORGANIC CHEMISTRY, UNIVERSITY OF NEW SOUTH WALES, BROADWAY, SYDNEY, AUSTRALIA. [*Received, November 25th*, 1958.]

---

588. *Sodium Derivatives of Dimethylstannane.*

By S. F. A. KETTLE.

Conductimetric titration of a solution of sodium in liquid ammonia with dimethylstannane shows the formation of dimethylstannylenedisodium, $SnMe_2Na_2$, dimethylstannylsodium, $SnMe_2HNa$, and *sym*-tetramethyldistannyldisodium, $(SnMe_2Na)_2$. Under suitable conditions aminodimethylstannylsodium, $Me_2(NH_2)SnNa$, is also formed. Dimethylstannylenedisodium reacts with ammonia above 0° to give aminodimethylstannylsodium. With methyl iodide it gives tetramethyltin [1] and with ammonium bromide, dimethylstannane. Dimethylstannylsodium, which has not been prepared pure, decomposes at 20° to give *sym*-tetramethyldistannyldisodium. *sym*-Tetramethyldistannyldisodium, which can be prepared pure and is stable at room temperature, reacts with ammonium bromide to give a mixture of dimethylstannane and dimethyltin, $(SnMe_2)_n$. With methyl iodide, hexamethyldistannane, Sn_2Me_6, is formed. Aminodimethylstannylsodium, which is stable at room temperature and can be prepared pure, reacts with ammonium bromide to give dimethyltin.

KRAUS and GREER reported that the reaction between dimethyltin dichloride and sodium in liquid ammonia proceeds with the successive formation of the yellow, insoluble dimethyltin, $(SnMe_2)_n$, the red soluble *sym*-tetramethyldistannyldisodium, $(SnMe_2Na)_2$, and ultimately the intensely red and soluble dimethylstannylenedisodium, $SnMe_2Na_2$.[1] In the work reported here the same compounds were obtained, but the last two have been found to be lime-green, the red colours reported by Kraus and Greer probably being caused by aminodimethylstannylsodium, $Me_2(NH_2)SnNa$.

The method of simultaneous measurement of conductivity and evolution of hydrogen in the titration of a solution of sodium in liquid ammonia with a volatile hydride was used to study the reaction between sodium and dimethylstannane.[2]

A typical variation of conductivity as successive portions of dimethylstannane were added to a solution of sodium in liquid ammonia at the temperature of melting chloroform (−63·5°) is shown in Fig. 1. The conductivity is a minimum when the $Na : SnMe_2H_2$ ratio is rather less than 2 : 1; at this point the blue colour of the solution was discharged, showing that the principal reaction is between two atoms of sodium and one molecule of dimethylstannane. The hydrogen evolution confirms that dimethylstannylenedisodium is formed:

$$SnMe_2H_2 + 2Na = SnMe_2Na_2 + H_2 \quad \ldots\ldots\ldots\ldots \quad (1)$$

In a competing reaction dimethylaminostannylsodium is formed, but this reaction is negligible under the conditions of the run. The conductivity becomes constant at an

[1] Kraus and Greer, *J. Amer. Chem. Soc.*, 1925, **47**, 2568.
[2] Emeléus and Kettle, *J.*, 1958, 2444.

$Na : SnMe_2H_2$ ratio of just less than 1 : 1, showing that the reaction between dimethylstannylenedisodium and dimethylstannane involves one molecule of each.

The evolution of hydrogen throughout the same titration is shown in Fig. 2. Up to $Na : SnMe_2H_2 = 2 : 1$ it is that required by eqn. (1) for the formation of dimethylstannylenedisodium. In Fig. 2 the broken line (1) is the plot expected if the reaction between dimethylstannylenedisodium and dimethylstannane proceeded with the formation of dimethylstannylsodium, $SnMe_2HNa$:

$$SnMe_2Na_2 + SnMe_2H_2 = 2SnMe_2HNa \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The broken line (2) is the plot expected if the reaction gave *sym*-tetramethyldistannyldisodium, $(SnMe_2Na)_2$:

$$SnMe_2Na_2 + SnMe_2H_2 = (SnMe_2Na)_2 + H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The experimental plot lies between (1) and (2), yet shows the abrupt cessation of hydrogen evolution required by equation (3) at $Na : SnMe_2H_2 = 1 : 1$ (when all of the dimethylstannylenedisodium formed as an intermediate has reacted); it is concluded that reactions (2) and (3) proceed simultaneously.

FIG. 1. *Variation of resistance in the titration of sodium in liquid ammonia with dimethylstannane.*

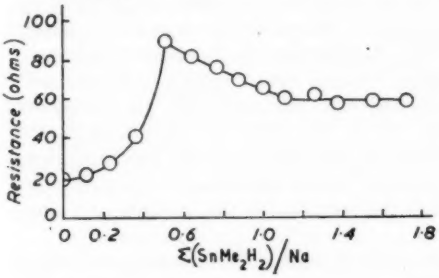
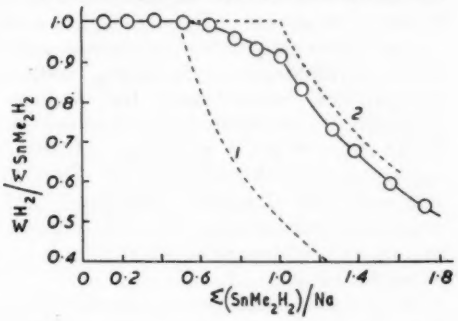


FIG. 2. *Evolution of hydrogen in the titration of sodium in liquid ammonia with dimethylstannane.*



When dimethylstannane and twice the equivalent amount of sodium, as a concentrated solution in liquid ammonia, are allowed to react rapidly at −45° the solution contains " excess " of sodium and more hydrogen is evolved than could have come from the dimethylstannane taken. The excess of hydrogen is equimolar with the excess of sodium. This clearly demonstrates that the solvent is participating in the reaction, an amino-group replacing a hydrogen atom in dimethylstannane, aminodimethylstannylsodium being formed:

$$SnMe_2H_2 + Na + NH_3 = Me_2(NH_2)SnNa + \tfrac{3}{2}H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Solid dimethylstannylenesodium evolved ammonia and hydrogen on warming to room temperature to give pure aminodimethylstannylsodium: $SnMe_2Na_2 + NH_3 = Me_2(NH_2)SnNa + NaH$. This reaction provides a convenient way of preparing pure aminodimethylstannylsodium. The composition of the product has been confirmed by analysis. Dimethylstannylenedisodium had presumably been left as an ammine at −63·5°; on warming, reaction occurred to give aminodimethylstannylsodium and sodium hydride. The hydrogen evolved came from the reaction between sodium hydride and ammonia giving hydrogen and sodamide.[3]

The aminodimethylstannylsodium dissolved in liquid ammonia to form an intensely red solution which gave only dimethyltin $(SnMe_2)_n$ on addition of ammonium bromide.

[3] Hurd, " Chemistry of the Hydrides," Wiley, 1952, p. 31. A subsidiary experiment has shown that this reaction proceeds slowly at room temperature between sodium hydride and gaseous ammonia.

Ammonium bromide also reacted with the remaining sodium hydride, giving hydrogen: $NaH + NH_4Br = NaBr + NH_3 + H_2$. The sum of this hydrogen and that liberated earlier by the reaction between sodium hydride and ammonia was equimolar with the dimethylstannylenedisodium taken, as required by the above reaction series.

When the solvent ammonia was removed at −63·5° from a mixture of dimethylstannylsodium and *sym*-tetramethyldistannyldisodium no hydrogen was evolved until the solid residue was warmed to 0°; at room temperature dimethylstannylsodium decomposed rapidly, one mole of hydrogen being evolved from two of the hydride. The solid residue completely dissolved in liquid ammonia giving a solution with the properties expected of pure *sym*-tetramethyldistannyldisodium, suggesting that this is the product of the decomposition of dimethylstannylsodium. This conclusion was confirmed by analysis: $2Me_2SnHNa = (SnMe_2Na)_2 + H_2$. *sym*-Tetramethyldistannyldisodium is stable at room temperature in the absence of air.

The reaction between dimethylstannylenedisodium and ammonium bromide in liquid ammonia at −63·5° regenerates dimethylstannane, identified by its molecular weight and infrared spectrum. Ammonia and dimethylstannane are best separated chemically by washing with 10% sulphuric acid.

When dimethylstannane and sodium react at −45° to give a high yield of aminodimethylstannylsodium, the addition of ammonium bromide gives dimethyltin in addition to dimethylstannane. The dimethyltin was characterised as described below.

sym-Tetramethyldistannyldisodium would be expected to give the unknown *sym*-tetramethyldistannane, $(SnMe_2H)_2$, with ammonium bromide in liquid ammonia. The products isolated from this reaction were dimethyltin and dimethylstannane; presumably *sym*-tetramethyldistannane is first formed but rapidly decomposes: $(SnMe_2H)_2 = SnMe_2 + SnMe_2H_2$. Dimethylstannane was removed with the ammonia and separated as described above. Dimethyltin, left in the solid residue, was extracted with methylene dichloride, centrifuged, and obtained pure by removing the methylene dichloride under vacuum. The yellow residue was identified by analysis and by a characteristic reaction with aqueous silver nitrate in which the particles of the insoluble tin compound turn black.

Methyl iodide and *sym*-tetramethyldistannyldisodium react in liquid ammonia to give hexamethyldistannane; after removal of the solvent the product remains in the solid residue. Dimethylstannylenedisodium and methyl iodide react to give tetramethyltin.[1]

In many of the reactions discussed above solid residues were obtained. In all cases an infrared spectrum of the solid was taken and in no case was Sn–H absorption found.

The chemistry of dimethylstannylsodium was not investigated since it was impossible to prepare it pure or in good yield.

Experimental

Dimethylstannane was prepared by the reduction of dimethyltin dichloride with lithium aluminium hydride in dioxan and purified by fractionation through a melting-toluene bath (−95°).[4] Dimethyltin dichloride (20·1 g.) and lithium aluminium hydride (5·1 g.) in 100 ml. of sodium-dry dioxan gave 9·0 g. of pure dimethylstannane (96% on $LiAlH_4$). The purity of the product was checked by vapour-pressure and molecular-weight measurements. The vapour pressure of dimethylstannane is given by the equation $\log_{10} p$ (cm.) = 6·64 − (1473/T), which gives b. p. 36° and Trouton constant 21·6.

The measurements of conductivity and hydrogen take-off were made at the temperature of melting chloroform (−63·5°),[2] the cell constant being 1·54. In this cell at −63·5° the conductivity of the solvent ammonia was $6{\cdot}85 \times 10^{-5}$ ohm^{-1} and the conductivity of a saturated solution of dimethylstannane in ammonia was $1{\cdot}45 \times 10^{-4}$ ohm^{-1}, both negligible compared with the conductivities measured in the run. Resistances were measured in a conventional bridge arrangement at 1000 c./sec. with oscilloscope display.[5] The typical run shown in Figs.

[4] Finholt, Bond, Wilzbach, and Schlesinger, *J. Amer. Chem. Soc.*, 1947, **69**, 2692.
[5] Haszeldine and Woolf, *Chem. and Ind.*, 1950, 544.

1 and 2 was made with 0·0165 g. of sodium in 3·13 g. of ammonia. The ammonia used was dried over sodium and the sodium was freshly cut reagent grade stored without oil.

Preparation and Properties of Dimethylstannylenedisodium.—Pure dimethylstannylenedisodium is made by adding small portions of dimethylstannane to sodium in liquid ammonia until a 1 : 2 ratio of hydride to sodium has been reached. Addition of the requisite amount of dimethylstannane in one portion invariably leads to the formation of a considerable amount of aminodimethylstannylsodium.

To sodium (0·352 mmole) in *ca.* 3 g. of ammonia frozen in liquid nitrogen, dimethylstannane (0·177 mmole) was added in portions and allowed to react at −63·5°. Hydrogen (0·177 mmole) was evolved. To sodium (0·943 mmole) in *ca.* 3 g. of ammonia frozen in liquid nitrogen, dimethylstannane (0·475 mmole) was added. The reaction vessel was warmed with the hand until all the ammonia had liquefied and then plunged into a bath of melting chlorobenzene (−45°). 0·615 mmole of hydrogen was evolved and the solution was still deep blue. After addition of just enough dimethylstannane to react with the remaining sodium the solution was reddish-brown. The hydrogen evolved indicates 59% formation of aminodimethylstannylsodium. The molecular weight of the hydrogen evolved in this reaction was 1·8 and its infrared spectrum showed no C–H adsorption, showing that no methane had been evolved, so that fission of a $Sn–CH_3$ bond had not taken place and the solvent must have participated in the reaction.

If sodium and dimethylstannane in an exact 2 : 1 ratio are allowed to react rapidly, then for every atom of hydrogen evolved in excess of that required by eqn. (1) there should also be one atom of sodium in excess [see eqn. (4)]. It is possible to determine the excess of sodium by adding ammonium bromide (by the rotating-arm technique) when for every atom of sodium one atom of hydrogen is liberated: $2NH_4Br + 2Na = 2NH_3 + 2NaBr + H_2$. In one run sodium (0·466 mmole) reacted with dimethylstannane to give hydrogen (0·252 mmole)—an "excess" of 0·019 mmole—and a dark blue solution which, with ammonium bromide, gave 0·018 mmole of hydrogen. In a second run sodium (0·391 mmole) reacted with dimethylstannane (0·196 mmole) to give hydrogen (0·209 mmole), an "excess" of 0·014 mmole, and a dark blue solution which with ammonium bromide gave 0·014 mmole of hydrogen.

After removal of the solvent ammonia by pumping at −63·5° for 2 3 hr., dimethylstannylenedisodium remains as a lime-green solid. On warming to room temperature it becomes dark red-brown, and ammonia and hydrogen are evolved. The ammonia evolved is not in a fixed ratio to the dimethylstannylenedisodium, varying from run to run. The hydrogen must have come from ammonia so a reaction between dimethylstannylenedisodium and the solvating ammonia is indicated: $SnMe_2Na_2 + NH_3 = Me_2(NH_2)SnNa + NaH$; $NaH + NH_3 = NaNH_2 + H_2$. The colour of the product suggests that it is aminodimethylstannylsodium. The hydrogen evolved is not equimolar with the dimethylstannylenedisodium taken, so sodium hydride must remain unchanged. This will react with ammonium bromide in liquid ammonia to give hydrogen: $NaH + NH_4Br = NaBr + NH_3 + H_2$, and the total hydrogen evolved should then be equimolar with the dimethylstannylenedisodium taken. Dimethylstannylenedisodium (0·146 mmole) liberated hydrogen (0·032 mmole) on warming to room temperature. Addition of ammonia and ammonium bromide caused the evolution of hydrogen (0·115 mmole). The total hydrogen liberated (0·147 mmole) is equimolar with the dimethylstannylenedisodium taken, confirming the above reaction scheme.

Kraus and Greer reported on the chemistry of (impure) dimethylstannylenedisodium but did not mention its reaction with ammonium halides.[1] In a previous paper a method of chemically separating stannane and the monoalkylstannanes from ammonia by use of a solution of copper sulphate in 10% sulphuric acid was described.[2] Dimethylstannane reacts very rapidly with copper sulphate to give a brown precipitate, so in the separation of dimethylstannane from ammonia, 10% sulphuric acid was used alone. A solution of pure dimethylstannylenedisodium (0·196 mmole) was prepared as described above and excess of ammonium bromide added by the rotating-arm technique. The volatile material was separated and ammonia removed from this chemically. After fractionation through a bath at −78° to remove water, the product was pure dimethylstannane (Found: *M*, 152. Calc. for $SnMe_2H_2$: *M*, 151), confirmed by its infrared spectrum and vapour pressure (5·4 mm. at −63·5°. $SnMe_2H_2$ has 5·2 mm. at −63·5°). Yield, 0·0097 g. (30%).

Preparation and Properties of Aminodimethylstannylsodium.—As described in the preceding section aminodimethylstannylsodium is made by the thermal decomposition of dimethylstannylenedisodium in the presence of ammonia. The product is contaminated by sodium

XUM

hydride and amide; if in the preparation the ammonia is removed slowly it is found that aminodimethylstannylsodium is left as a hard film on the sides of the reaction vessel and the contaminants are left as a white residue at the bottom. Prepared and separated in this way a specimen of aminodimethylstannylsodium was analysed (Found: C, 13·1; H, 4·5; N, 7·6. Calc. for SnC_2H_8NNa: C, 12·8; H, 4·3; N, 7·5%).

With ammonium bromide in liquid ammonia, aminodimethylstannylsodium gave a yellow precipitate of dimethyltin. The volatile material could not be resolved into fractions and was completely absorbed by 10% sulphuric acid. The yellow residue was partially soluble in water giving a solution which contained sodium and ammonium bromides. The particles of yellow, water-insoluble precipitate, when added to neutral silver nitrate solution, turned black, a reaction characteristic of dimethyltin. Dimethyltin dissolved in methylene dichloride to give a yellow solution which was freed from ionic halides by centrifuging. Aminodimethylstannylsodium (0·226 mmole), after reaction with ammonium bromide in liquid ammonia, gave 0·0256 g. of methylene dichloride-soluble material (Found: C, 16·5; H, 3·8. Calc. for SnC_2H_6: C, 16·1; H, 4·0%).

Aminodimethylstannylsodium is best stored in a vacuum. When opened in a nitrogen-flushed dry-box a specimen turned dark-green in 15 min. and was black after ½ hr. After two days the black residue was analysed (Found: C, 6·4; H, 3·7; N, 5·3. Calc. for SnC_2H_8NNa: C, 12·8; H, 4·3; N, 7·5%).

Preparation and Properties of sym-*Tetramethyldistannyldisodium.*—*sym*-Tetramethyldistannyldisodium is the major product of the reaction between equimolar quantities of dimethylstannylenedisodium and dimethylstannane. Dimethylstannylsodium, which is also formed, decomposes on warming to give *sym*-tetramethyldistannyldisodium and hydrogen. Dimethylstannylenedisodium (0·278 mmole) reacted with dimethylstannane (0·281 mmole) in liquid ammonia to give hydrogen (0·226 mmole), indicating the 81% formation of *sym*-tetramethyldistannyldisodium. On standing at −63·5° for ½ hr. no more hydrogen was liberated, showing that the decomposition of dimethylstannylsodium does not occur at this temperature. After removal of the solvent ammonia the solid product was slowly warmed. At −10° hydrogen evolution commenced and at 20° was rapid. In the decomposition 0·065 mmole of hydrogen was evolved, a total of 0·281 mmole, equimolar with the dimethylstannylenedisodium taken. After removal of ammonia the product was analysed (Found: C, 14·2; H, 3·8.. Calc. for $Sn_2C_4H_{12}Na_2$: C, 14·0; H, 3·5%). The product was deposited as a thin hard film on the walls of the reaction vessel, difficult to remove with a spatula.

With methyl iodide, *sym*-tetramethyldistannyldisodium gave hexamethyldistannane. Excess of methyl iodide was condensed on a frozen solution of *sym*-tetramethyldistannyldisodium (0·302 mmole). A white precipitate of sodium iodide was formed on warming. Removal of the volatile material at −45° followed by methylene dichloride extraction of the solid residue, centrifuging, and removal of the solvent *in vacuo*, gave a white oily solid, m. p. 22° (lit.,[6] Sn_2Me_6, m. p. 23°) (Found: C, 21·8; H, 5·2. Calc. for $Sn_2C_6H_{18}$: C, 22·0; H, 5·5%).

sym-Tetramethyldistannyldisodium reacted with ammonium bromide in liquid ammonia to give dimethyltin and dimethylstannane, separated as described above. *sym*-Tetramethyldistannyldisodium (0·222 mmole) gave 0·0353 g. of dimethyltin (Found: C, 16·3; H, 3·4. Calc. for SnC_2H_6: 0·0330 g. containing C, 16·1; H, 4·0%), and 0·0060 g. (18%) of dimethylstannane [*M*, 154 (calc., 151)], confirmed by its infrared spectrum and vapour pressure (5·3 mm. at −63·5°; $SnMe_2H_2$ has 5·2 mm. at −63·5°). The low yield of dimethylstannane is attributed to the difficulty of separation from ammonia.

sym-Tetramethyldistannyldisodium does not react with dimethylstannane; in liquid ammonia the latter separates as a liquid (sometimes colloidal) and can be recovered.

sym-Tetramethyldistannyldisodium is best stored in a vacuum; it rapidly decomposes in a nitrogen-flushed dry-box, presumably by reacting with traces of oxygen.

Infrared Spectra.—The infrared spectra of all the stable compounds made above were recorded. Aminodimethylstannylsodium and dimethylstannylenedisodium appeared to react with all the media used (hexachlorobutadiene, Nujol, potassium bromide—with the last two because of traces of water and air). The spectra recorded, while perhaps not those of the compounds, showed the expected absorption, *i.e.*, N–H, C–H. The infrared spectrum of dimethylstannane showed the following peaks in the range 4000—600 cm.$^{-1}$: 3666 cm.$^{-1}$ (w),

[6] Kraus and Bullard, *J. Amer. Chem. Soc.*, 1926, **48**, 2132.

3070 (m), 3014 (s), 2938 (s), 2838 (m), 2622 (vw), 2395 (w), 2204 (w), 1993 (vw), 1856 (vs), 1738 (w), 1727 (w), 1531 (w), 1430 (w), 1348 (vw), 1304 (vw), 1212 (w), 1204 (w), 1195 (w), 1140 (vw), 1063 (vw), 773 (vs), 755 (vs), 744 (vs), 721 (vs), 708 (vs).

The author is indebted to Professor H. J. Emeléus, C.B.E., F.R.S., for advice and encouragement and to the Department of Scientific and Industrial Research for a Maintenance Grant.

UNIVERSITY CHEMICAL LABORATORY,
LENSFIELD ROAD, CAMBRIDGE.

[*Received, December* 11*th*, 1958.]

---

589. *The Reaction of* 1-*Nitromethylcycloheptene with Selenium Dioxide.*

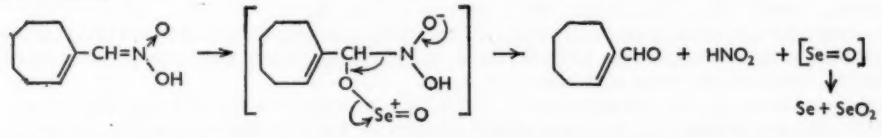
By Z. ECKSTEIN, A. SACHA, T. URBAŃSKI, and (MRS.) H. WOJNOWSKA-MAKARUK.

1-Nitromethylcycloheptene and selenium dioxide give 1-formylcycloheptene and cyclohept-1-enecarboxylic acid.

THE only record of the action of selenium dioxide on nitroalkanes is the statement, without experimental details, by Rabjohn and Harjes,[1] that nitromethane in dioxan gives formic acid. We have studied the reaction of 1-nitromethylcycloheptene [2] which might have been expected to introduce a hydroxyl group in the α-position to the double bond. The reaction was carried out in organic solvents in presence of a small quantity of water or in acetic anhydride. However, the reaction in ethanol gave 1-formylcycloheptene (33%) and cyclohept-1-enecarboxylic acid (14·3%); in dioxan the same products were formed (40·5% and 6·4% respectively; total conversion in both cases *ca.* 47%); in acetic anhydride, 16% of the aldehyde was obtained. The acid was probably formed *via* the aldehyde since similar oxidations by selenium dioxide are known; [3] we also effected the oxidation by silver oxide.

The aldehyde and acid have both been prepared before,[4] by less convenient methods. The structures are confirmed by the infrared spectra: The aldehyde has bands at 2710 (CHO[5]), 1678 (αβ-unsaturated C=O), and 1639 sh (C=C[5]) cm.$^{-1}$. The acid gives an ester with bands at 1703 (αβ-unsaturated CO_2R [6]), 1641 (C=O), 1250 and 1199 (C–O stretching of C:C·CO_2R [6,7]) cm.$^{-1}$. Both aldehyde and ester give C–H stretching bands at 2922 (asymm.) and 2848—2850 (symm.) and 1444—1447 cm.$^{-1}$ (scissors vibration of CH_2, slightly shifted, probably because of the large ring [8]).

In all the oxidations, nitrous fumes are evolved. The reaction may occur as illustrated.



The reaction may have practical interest as the acid has cholagogic properties.[9]

[1] Rabjohn and Harjes, "Organic Reactions," Wiley & Sons, New York, 1949, Vol. V, p. 331.
[2] Eckstein, Sacha, and Urbański, *Bull. Acad. polon. Sci., Cl. III*, 1957, **5**, 213.
[3] Rabjohn, "Organic Reactions," Wiley & Sons, New York, 1949, Vol. V.
[4] Wallach, *Annalen*, 1906, **345**, 152; Braude and Evans, *J.*, 1955, 3334; Spiegel, *Annalen*, 1882, **211**, 119; Willstätter, *Ber.*, 1898, **31**, 2506; Braren and Bachner, *Ber.*, 1900, **33**, 685.
[5] Pinchas, *Analyt. Chem.*, 1957, **29**, 334.
[6] Bellamy, "Infra-red Spectra of Complex Molecules," Methuen, London, 1958.
[7] Brugel, "Einführung in die Ultrarotspektroskopie," Steinkopff, Darmstadt, 1954.
[8] Jones and Sandorfy, "Chemical Applications of Spectroscopy," Interscience Publ. Inc., New York, 1956, p. 361.
[9] G.P. 1,005,062; *Chem. Zentr.*, 1958, 11,317.

XUM

Experimental

Reaction in Dioxan.—Selenium dioxide (0·2 mole, 22·2 g.) in dioxan (175 ml.) and water (7 ml.) was added during 1 hr. to a stirred solution of 1-nitromethylcycloheptene (0·2 mole, 31 g.) in dioxan (60 ml.) on a boiling water bath, and the whole was stirred there for 2—3 hr. Then, after filtration, the dioxan was removed at 60° under reduced pressure and the residue distilled in steam. The first part of the distillate (*ca.* 350 ml.) contained the aldehyde as an oil; later parts (*ca.* 500 ml.) contained crystals of the acid.

The distillate containing the aldehyde was saturated with salt and extracted with ether (4 × 35 ml.), and the extracts were dried (Na_2SO_4) and evaporated. Distillation gave the aldehyde, b. p. 70—95° (10 g., 40·5%), which after redistillation had b. p. 86—92°/10 mm., n_D^{20} 1·4792. Analysis did not show nitrogen in this product but presence of unchanged nitro-compound was disclosed by an infrared band at 1563 cm.$^{-1}$. This product gave a 2,4-dinitrophenylhydrazone, m. p. 210—212° (from acetone) (Braude and Evans [4] give m. p. 210—211°) (Found: N, 18·3. Calc. for $C_{14}H_{16}O_4N_4$: N, 18·4%), and a semicarbazone, m. p. 204—205° (lit.,[4] m. p. 203—204° and 210—211°) (Found: N, 23·1. Calc. for $C_9H_{15}ON_3$: N, 23·2%).

The above aldehyde (28·3 g.) in alcohol (225 ml.) at 13° was treated dropwise with sodium metabisulphite (30·4 g.) in water (225 ml.) (temperature rise to 21°) and stirred at 13° for 5 hr. The precipitate was filtered off and washed with ether. 11·5 g. of it were decomposed with sodium carbonate (7·5 g.) in water (75 ml.). The aldehyde, recovered with ether, had b. p. 80—81°/15 mm., n_D^{20} 1·4922) (3·5 g.), and gave only a very weak infrared nitro-band.

With semicarbazide hydrochloride (22·3 g.) and crystalline sodium acetate (33·5 g.) in water (210 ml.) the crude aldehyde gave, in 4 hr., 75% of semicarbazone, m. p. 198—201°. This was steam-distilled with oxalic acid (25·2 g.) in water (100 ml.). Recovery of the aldehyde from the distillate as above gave 85·5% of material, b. p. 91—92°/24 mm., n_D^{20} 1·4998, which gave no nitro-band in the infrared spectrum.

The acid was recovered from the original steam-distillate by saturation with salt and extraction with ether (3 × 50 ml.), then removed from the ether by aqueous sodium carbonate and precipitated therefrom by acidification. The crude acid (1·8 g., 6·4%; m. p. 48—50°) recrystallised from 1 : 2 aqueous alcohol (1 g. per 15 ml.) and then had m. p. 51—52° (lit.,[4] m. p. 49—51° to 53—54°).

With thionyl chloride cyclohept-1-enecarboxylic acid gave its acid chloride (95·5%), b. p. 120°/30 mm., d_4^{20} 1·1264, n_D^{20} 1·5120, and thence by concentrated aqueous ammonia the amide, m. p. 125—126° (lit.,[10] m. p. 126°) (Found: N, 10·3. Calc. for $C_8H_{13}ON$: N, 10·1%).

Removing water during 24 hr. azeotropically from a boiling mixture of the acid (4·9 g.), ethyl alcohol (7 ml.), benzene (21 ml.), and concentrated sulphuric acid (0·49 g.), evaporation under reduced pressure, and distillation gave the ester, b. p. 118°/27 mm., d_4^{20} 0·9910 (Braren and Bachner [4] give b. p. 106—116°/14 mm.). The same ester was obtained from the acid chloride and ethyl alcohol.

The aldehyde had infrared bands at 3348vw, 3048sh, 2922vs, 2848s, 2710m, 1678vs, 1639vs, 1522vw, 1444s, 1400m, 1380m, 1359w, 1316m, 1272m, 1231s, 1184s, 1141m, 1131w, 1097m, 1075m, 1003w, 967m, 953m, 894m, 859s, 797m, and 731m cm.$^{-1}$.

The ester had infrared bands at 2973sh, 2922vs, 2850s, 1703vs, 1641s, 1547vw, 1447s, 1364m, 1328vw, 1278s, 1250vs, 1213m, 1199vs, 1172sh, 1147s, 1112m, 1094m, 1067s, 1028s, 997w, 969w, 950vw, 903vw, 853m, 784m, and 746s cm.$^{-1}$.

Reaction in Alcohol.—Selenium dioxide (22·2 g.) in anhydrous (35 ml.) and 95% alcohol (110 ml.) was added in 1 hr. to a stirred solution of 1-nitromethylcycloheptene in boiling anhydrous alcohol (60 ml.), and the whole stirred for 7 hr., then cooled, filtered, and evaporated under reduced pressure. Steam-distillation, etc., as before, gave the aldehyde [8·1 g., 32·7%; identified by its derivatives (mixed m. p.s)] and the acid (4·0 g., 14·3%).

Reaction in Acetic Anhydride.—Selenium dioxide (8·3 g.) was added in portions of *ca.* 2 g. to 1-nitromethylcycloheptene in acetic anhydride at 50°, and the whole stirred at 90° for 11 hr. Next morning the solid was filtered off and extracted with ether. The ether extract yielded 2 g. (16%) of aldehyde which was identified as above.

Oxidation of the Aldehyde to the Acid.—1-Formylcycloheptene (37·3 g.) was boiled with a solution of freshly prepared silver oxide in aqueous ammonia for 3 hr. After filtration the

[10] Bachner and Jacobi, *Ber.*, 1898, **31**, 2004; Bachner, *Ber.*, 1899, **32**, 705.

solution was acidified with 50% sulphuric acid and distilled in steam. Recovery of cyclohept-1-enecarboxylic acid from the distillate by means of ether and crystallisation from aqueous alcohol gave an acid (0·85 g., 20%), m. p. and mixed m. p. 51—52°.

The authors are indebted to Mr. P. Gluziński for determining the infrared spectra.

DEPARTMENT OF ORGANIC TECHNOLOGY,
INSTITUTE OF TECHNOLOGY (POLITECHNIKA),
WARSAW, POLAND.

[*Received, December 23rd*, 1958.]

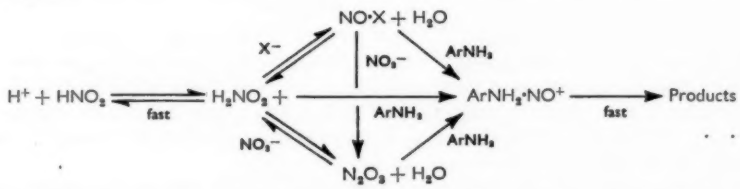
---

590. *Mechanism of the Azide–Nitrite Reaction. Part I.*

By G. STEDMAN.

Nitrous acid and hydrazoic acid react in the presence of excess of perchloric acid at 0° by two main paths. One involves formation of nitrosyl azide by a nucleophilic attack of the azide ion on dinitrogen trioxide; the other involves formation of nitrosyl azide by a nucleophilic attack of hydrazoic acid on the nitrous acidium ion. In each case nitrosyl azide subsequently breaks down rapidly to nitrogen and nitrous oxide. The results are in good agreement with the general theory of nitrosation in diazotisation and deamination put forward by Hughes, Ingold, and Ridd.[1] No evidence for nitrosation by the nitrosonium ion was found.

HUGHES, INGOLD, and RIDD[1] showed that a consistent account of the mechanism of diazotisation and deamination in dilute mineral acid is given by the following series of reactions. Similar schemes should apply to reactions of nitrous acid with other nucleophilic reagents.



. . . (1)

In this scheme there are two possible rate-determining steps. One is the formation of a nitrosating agent, the other is the reaction between the nitrosating agent and the substrate, in this case an amine. Which step is rate determining in any particular case depends on the concentration and reactivity of the free amine. The nitrosamine that is obtained as the primary product undergoes a subsequent rapid rearrangement and reaction to give the final products. Hughes, Ingold, and Ridd showed that the nitrous acidium ion, dinitrogen trioxide, nitrosyl iodide, nitrosyl bromide, and nitrosyl chloride could all act as nitrosating agents.[1] They were unable to find evidence for nitrosation by the nitrosonium ion, the most reactive of possible nitrosating agents, under the mildly acid conditions they used (pH $\approx$2).

Seel and Schwaebel studied the kinetics of the reaction between nitrous acid and hydrazoic acid in acetate buffers:[2]

$$HNO_2 + HN_3 \longrightarrow N_2 + N_2O + H_2O \quad . . . . . (2)$$

They found that the rate of reaction was independent of the concentration of the azide, and could be fitted to the rate law $v = k[H^+]^2[NO_2^-]$. This result was interpreted as

[1] Hughes, Ingold, and Ridd, *J.*, 1958, 58.
[2] Seel and Schwaebel, *Z. anorg. Chem.*, 1953, **274**, 169.

XUM

showing that reaction occurred by a rate-determining formation of the nitrosonium ion from the nitrous acidium ion, followed by a rapid reaction with azide ions:

$$H_2NO_2^+ \xrightarrow[\text{slow}]{} NO^+ + H_2O \xrightarrow[\text{fast}]{N_3^-} N_2NO \xrightarrow[\text{fast}]{} N_2 + N_2O \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Bunton, Llewellyn, and Stedman showed that Seel and Schwaebel's results could equally well be explained as a rate-determining formation of nitrosyl acetate, which reacted rapidly with azide in a subsequent fast step: [3]

$$CH_3{\cdot}CO_2^- + H_2NO_2^+ \xrightarrow[\text{slow}]{} CH_3{\cdot}CO_2{\cdot}NO + H_2O \xrightarrow[\text{fast}]{N_3^-} N_3{\cdot}NO + CH_3{\cdot}CO_2^- \xrightarrow[\text{fast}]{} N_2 + N_2O \quad (4)$$

It was decided to investigate the reaction between nitrous acid and hydrazoic acid in the absence of nucleophilic buffers for evidence of the nitrosonium ion as a reaction intermediate. In the present work solutions were buffered with an excess of perchloric acid. The perchlorate ion is a very weak nucleophilic reagent, and does not intervene chemically in the mechanism of diazotisation and deamination.[1]

There is much evidence from kinetic studies that nucleophilic anions and nitrous acid interact to form nitrosyl compounds in aqueous solution.[1,3] Measurements of the visible-light absorption of solutions of nitrous acid in concentrated hydrochloric acid, nitric acid, and perchloric acid lead to the same conclusion.[3,4] Lucien has recently isolated nitrosyl azide in low yield at low temperatures.[5] It readily breaks down to nitrogen and nitrous oxide. Clusius and Effenberger have shown by means of labelling with nitrogen-15 that the nitrogen and nitrous oxide formed in the reaction between nitrous acid and hydrazoic acid have the isotopic composition corresponding to nitrosyl azide's being a reaction intermediate: [6]

$$\overset{a}{H}-\overset{b}{N}=\overset{a}{N}=\overset{c}{N} + \overset{c}{HNO_2} \longrightarrow \overset{a}{N}=\overset{b}{N}-\overset{a}{N}=\overset{c}{N}-O \longrightarrow \overset{a}{N}\equiv\overset{b}{N} + \overset{a}{N}\leftarrow\overset{c}{N}=O \quad . \quad . \quad . \quad . \quad (5)$$

On the basis of this evidence, the present results were interpreted by assuming that nitrosyl azide was formed in the reaction, and that this rapidly broke down to nitrogen and nitrous oxide. Evidence to be presented later shows that the breakdown of nitrosyl azide to the reaction products in aqueous solution is much more rapid than the rate of hydrolysis by solvent. The various forms of rate equation observed were interpreted in terms of different mechanisms all leading to the formation of nitrosyl azide.

Results.—The kinetics of reaction were studied at several concentrations of excess of perchloric acid from 0·0029 to 0·173M, equimolar amounts of nitrous and hydrazoic acid being used. By varying the initial concentration of the reactants, the total order of reaction with respect to both components was found. The appropriate equation is

$$\log t_{\frac{1}{2}} = C - (n - 1) \log [a]$$

where n is the overall kinetic order, [a] is the initial concentration of each reactant, $t_{\frac{1}{2}}$ is the half-life of the reactants, and C is a constant.[1] The results, given in Table 1, show that the reaction is of second order over the acidity range studied. Second-order rate constants are also given.

The second-order rate constants for these runs and also for a number of runs carried out at other acidities, given in Table 4, are plotted against $[H^+]$ in the Figure. The second-order rate constants, k_2, were calculated from the normal integrated form of the rate equation. Reaction is clearly acid catalysed. Below $[H^+] = 0{\cdot}04$M, $k_2 = 0{\cdot}80 + 33{\cdot}7$ $[H^+]$ sec.$^{-1}$ mole^{-1} l.; above $[H^+] = 0{\cdot}10$M, $k_2 = 33{\cdot}7$ sec.$^{-1}$ mole^{-1} l. The reason for this change in the dependence of k_2 on $[H^+]$ is given later.

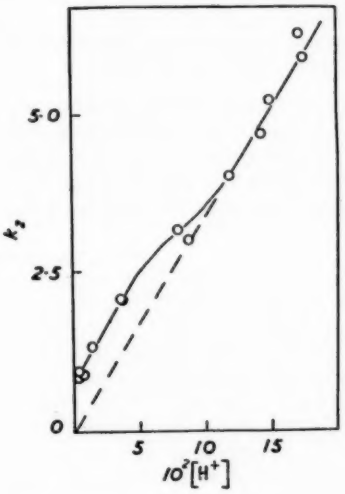
[3] Bunton, Llewellyn, and Stedman, *Spec. Publ. Chem. Soc.*, No. 10, p. 113.
[4] Schmid and Maschka, *Z. physik. Chem.*, 1941, **49**, *B*, 171.
[5] Lucien, *J. Amer. Chem. Soc.*, 1958, **80**, 4458.
[6] Clusius and Effenberger, *Helv. Chim. Acta*, 1955, **38**, 1834.

TABLE 1. *Dependence of total reaction order on acidity at 0°.*

$10^3[H^+]$ (M)	0·29	1·42	3·64	7·9	17·3
10^3[a] (M)	2·00	2·04	2·04	0·800	0·851
$t_{1/2}$ (sec.)	744	357	240	372	204
10^3[a] (M)	0·800	0·407	0·407	0·160	0·341
$t_{1/2}$ (sec.)	1735	1830	1332	1842	456
10^3[a] (M)	0·400	—	—	—	—
$t_{1/2}$ (sec.)	3440	—	—	—	—
Total reaction order, *n*	2·0	2·0	2·1	2·0	1·9
k_2 (mean) (sec.$^{-1}$ mole^{-1} l.)	0·85	1·41	2·13	3·14	6·34

[a] = $[HNO_2]$ = $[HN_3]$.

Reaction at Low Concentrations of Excess of Perchloric Acid.—The order of reaction with respect to the individual components, nitrous acid and hydrazoic acid, was determined by varying the relative concentrations of each, and comparing the initial rates of reaction. The results are given in Table 2.



Azide–nitrite reaction: second-order rate constant as a function of excess of perchloric acid concentration.

TABLE 2. *Initial rates of reaction at low acidity.* 0°.

Run No.	21	22	23	24	29	30
$10^4[HN_3]$	4·02	1·61	1·61	4·02	20·00	4·00
$10^4[HNO_2]$	8·04	8·04	4·02	4·02	4·00	4·00
$10^3[H^+]$	2·32	2·32	2·32	2·32	4·7	4·7
$10^7 v_0$ (sec.$^{-1}$ mole l.$^{-1}$)	4·8	4·7	0·83	1·1	1·71	1·23

v_0 = Initial rate.

The reaction is of second order in nitrous acid, and nearly of zero order in hydrazoic acid, *i.e.*, $v = k_2[HNO_2]^2$. The slight dependence of rate on azide concentration is a real effect, due to a small amount of reaction going by a mechanism with a rate equation $v = k_3^{HN_3}[H^+][HNO_2][HN_3]$. It is this mechanism that is responsible for the acid catalysis of the reaction.

The rate equation $v = k_2[HNO_2]^2$ is interpreted as a rate-determining formation of dinitrogen trioxide, followed by a rapid reaction with either azide ion or hydrazoic acid:

$$NO_2^- + H_2NO_2^+ \xrightarrow[\text{slow}]{} N_2O_3 + H_2O \xrightarrow[\text{fast}]{\text{azide}} N_3{\cdot}NO + NO_2^- \xrightarrow[\text{fast}]{} N_2 + N_2O \quad . \; . \; . \quad (6)$$

The formation of dinitrogen trioxide from two molecules of nitrous acid has been written as a nucleophilic substitution of a nitrite ion at the nitrous acidium ion, the form suggested

by Hughes, Ingold, and Ridd.[1] It differs from the conventional formulation shown in eqn. (7), only in a rapid, pre-equilibrium proton transfer. The rate of reaction (6) is given by $v = k_3^{NO_2^-}[H^+][HNO_2][NO_2^-]$, where $k_3^{NO_2^-} = k_2/K_{HNO_2}$ and K_{HNO_2} is the dissociation constant of nitrous acid.

$$2HNO_2 \longrightarrow N_2O_3 + H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

A comparison of the second-order rate constants, k_2, for the formation of dinitrogen trioxide, obtained by a number of workers is shown in Table 3.

TABLE 3. *Second-order rate constants for the formation of dinitrogen trioxide at* 0°.

	$[HNO_2]$ (M)	μ (M)	k_2 (sec.$^{-1}$ mole^{-1} l.)	Ref.
Diazotisation of aniline	0·001	0·01	0·85	*a*
Diazotisation of aniline			0·92	*b*
Diazotisation of other aromatic amines	0·001	0·01	0·80	*c*
Diazotisation in acetate and phthalate buffers	0·0002	0·1	0·78	*a*
Oxygen exchange between nitrous acid and water	0·01—0·1	0·3—2·0	0·5	*d*
Azide–nitrite reaction	0·002	0·01	0·80	This paper

μ = Ionic strength.

References: *a*, ref. 1. *b*, Schmid and Woppmann, *Monatsh.*, 1952, **83**, 346. *c*, Larkworthy, personal communication. *d*, ref. 3.

The kinetic form of the rate equation, and the agreement between the second-order rate constant obtained in this work and those found in other investigations are sufficient to establish that a rate-determining formation of dinitrogen trioxide is involved.

The subsequent fast step in which dinitrogen trioxide reacts with azide to form nitrosyl azide involves the azide ion, and not hydrazoic acid:

$$N_3^- + N_2O_3 \longrightarrow N_3{\cdot}NO + NO_2^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

This is shown by the dependence of the rate of reaction on acidity. If the reaction path is that described above, then the occurrence of a rate-determining formation of dinitrogen trioxide depends on there being a sufficiently high concentration of the reacting azide species to trap all of the molecules formed in eqn. (6). Hydrazoic acid is a weak acid: $K_a = 1{\cdot}0 \times 10^{-5}$ mole l.$^{-1}$ at 0°.[7] In our work the presence of excess of perchloric acid ensured that nearly all of the azide was present as undissociated hydrazoic acid. On increasing the concentration of excess of perchloric acid the concentration of hydrazoic acid remains essentially unaltered, while that of the azide ion decreases inversely. Thus, if dinitrogen trioxide reacts with hydrazoic acid increasing acidity will have no effect on the rate of reaction. If dinitrogen trioxide reacts with azide ion, then on increasing the acidity sufficiently a point will be reached where the concentration of azide ions will not be great enough to trap all of the dinitrogen trioxide molecules formed; some will react with water, and the reaction rate will decrease. In the limiting case nearly all of the dinitrogen trioxide molecules will react with water, and only a small fraction with azide ions. The mechanism will then be of the form shown in eqn. (9), the rate law will be $v = k_3[HNO_2]^2[N_3^-]$, and the specific rate will drop to a low value.

$$NO_2^- + H_2NO_2^+ \underset{\text{fast}}{\rightleftharpoons} N_2O_3 + H_2O$$

$$N_2O_3 + N_3^- \underset{\text{slow}}{\longrightarrow} N_3{\cdot}NO + NO_2^-$$

$$N_3{\cdot}NO \underset{\text{fast}}{\longrightarrow} N_2 + N_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

The "kink" in the plot of k_2 against $[H^+]$ (Figure) is due to just such a factor, reduction of the azide ion concentration below the critical value needed to compete effectively with water for dinitrogen trioxide, and corresponds to a change from the second-order kinetic

[7] Stedman, following paper.

XUM

form $v = k_2[HNO_2]^2$ to the third-order form $v = k_3[HNO_2]^2[N_3^-]$. The reason that the overall kinetics of the reaction between nitrous acid and hydrazoic acid remain of second order, as shown in Table 1, is that the transition from second-order to third-order kinetics for reaction *via* dinitrogen trioxide is accompanied by a large decrease in the specific rate, and this is overshadowed by the large contribution to the total rate due to another mechanism with a rate equation $v = k_3^{HN_3}[H^+][HNO_2][HN_3]$ which is also of second order with respect to the reagents. A similar change in kinetic form is observed in the diazotisation of aniline in dilute perchloric acid, on varying the acidity.[1]

As explained above, it is impossible to isolate the third-order rate equation, for reaction between an equilibrium concentration of dinitrogen trioxide and azide ions. To do so, it would be necessary to work with a very low concentration of azide ions, less than 10^{-7}M. This would entail working at a high acidity to suppress the ionisation of hydrazoic acid sufficiently, and under these conditions there would be a large contribution to the total rate by a mechanism with a rate equation $v = k_3^{HN_3}[H^+][HNO_2][HN_3]$. It is, however, possible to form an estimate of the relative reactivities of water and azide ion towards dinitrogen trioxide. From the Figure it can be seen that the transition from second order to third-order kinetics occurs between $[H^+] = 0{\cdot}04$ and $[H^+] = 0{\cdot}12$M. The mid-point of this range is $[H^+] = 0{\cdot}08$M and the average azide concentration for these experiments was *ca.* 0·0004M. Nearly all of this was present as hydrazoic acid. Knowing the dissociation constant of hydrazoic acid,[7] one can calculate that the value of $[N_3^-]$ is *ca.* 10^{-7}M. This concentration competes with approximately equal effectiveness to 55·5M-water for dinitrogen trioxide. The rates of reaction being assumed proportional to the concentrations of the reacting species, the relative reactivities of water and of the azide ion towards dinitrogen trioxide are $(10^{-7}/55{\cdot}5) : 1$; *i.e.*, $2 \times 10^{-9} : 1$. This value may be regarded only as an estimate of order of magnitude.

The Acid-catalysed Reaction.—The previous discussion has shown that up to $[H^+] = 0{\cdot}04$M, there is a constant contribution to the rate of reaction of $0{\cdot}80[HNO_2]^2$, because at these low acidities, and at the azide concentrations used, there was a sufficient concentration of azide ions to trap all of the dinitrogen trioxide formed. Above $[H^+] = 0{\cdot}12$M this mechanism makes a negligible contribution to the total rate under the conditions used (equal concentrations of nitrous acid and hydrazoic acid). Table 4 contains the observed second-order rate constants including corrections for reaction *via* dinitrogen trioxide. The corrected rate constants k_2^* are those for the acid-catalysed reaction.

TABLE 4. *Acid catalysis of the azide–nitrite reaction* 0°.

$10^3[H^+]$ (M)	2·3	2·9	14·2	36·4	37·1	79
k_2 (sec.$^{-1}$ mole^{-1} l.)	0·98	0·85	1·41	2·13	2·12	3·14
k_2^* sec.$^{-1}$ mole^{-1} l.)	0·18	0·05	0·61	1·33	1·32	2·34
$10^3k_2^*/[H^+]$ (sec.$^{-1}$ mole^{-2} l.^{2})	—	—	4·3	3·7	3·6	—
$10^3[H^+]$ (M)	88	120	143	149	173	176
$k_2 = k_2^*$ (sec.$^{-1}$ mole^{-1} l.)	3·0	4·07	4·75	5·23	6·33	5·90
$k_2^*/[H^+]$ (sec.$^{-1}$ mole^{-2} l.^{2})	—	3·4	3·3	3·5	3·7	3·4

$k_2^* = k_2 - 0{\cdot}8[HNO_2]^2$ for $[H^+] < 0{\cdot}04$M. $k_2^* = k_2$ for $[H^+] > 0{\cdot}12$M. $[HNO_2] = [HN_3] =$ 0·0002 — 0·0004M.

The results show that the rate equation for the acid-catalysed reaction is $v = k_2[H^+][\text{Reactant}]^2$, where $[\text{Reactant}] = [HNO_2] = [HN_3]$. In order to obtain the order with respect to the individual components, it is necessary to vary their relative concentrations. Table 5 contains some results for experiments in which this was done. Pairs of runs were

TABLE 5. *Order of the acid-catalysed reaction with respect to individual components.*

$10^3[H^+]$ (M)	3·27	3·27	13·45	13·45	17·26	17·26
$10^4[HN_3]$ (M)	2·84	1·42	12·5	2·5	17·3	3·45
$10^4[HNO_2]$ (M)	2·84	2·84	2·5	2·5	3·46	3·46
10^6v_0 (sec.$^{-1}$ mole l.$^{-1}$)	0·069 *	0·034 *	1·44	0·24	3·22	0·69

v_0 = initial rate. * Values corrected for reaction *via* dinitrogen trioxide.

carried out at various concentrations of excess of perchloric acid, in which the value $[HNO_2]$ was kept constant, while $[HN_3]$ was varied. The initial rates of reaction were then compared.

These results show that at $[H^+] = 0{\cdot}173$, $0{\cdot}1345$, and $0{\cdot}0327$M, the acid-catalysed reaction is of first order in $[HN_3]$. [For measurements at $0{\cdot}0327$M-acid, it was necessary to correct the observed initial rate for reaction *via* a rate-determining formation of dinitrogen trioxide, of $v = 0{\cdot}8[HNO_2]^2$ (sec.$^{-1}$ mole l.$^{-1}$).] As the total reaction order is two, as shown in Table 1, the full rate equation is $v = k_3^{HN_3}[H^+][HNO_2][HN_3]$ with $k_3^{HN_3} = 33{\cdot}7$ sec.$^{-1}$ mole^{-2} l.^{2}.

This rate equation corresponds to a mechanism in which the rate-determining step is a bimolecular reaction between hydrazoic acid and the nitrous acidium ion:

$$H_2NO_2^+ + HN_3 \xrightarrow[\text{slow}]{} N_3{\cdot}NO + H_3O^+ \xrightarrow[\text{fast}]{} N_2 + N_2O + H_3O^+ \quad . \quad . \quad . \quad . \quad . \quad (10)$$

This mechanism is formally similar to that found by Hughes, Ingold, and Ridd for the diazotisation of *o*-chloroaniline in dilute perchloric acid.[1] Hydrazoic acid appears to be a weaker nucleophilic reagent towards the nitrous acidium ion than is *o*-chloroaniline, the third-order rate constant for the latter being 175 sec.$^{-1}$ mole^{-2} l.^{2}. It is important to establish that the acid catalysis of the azide nitrite reaction is due to reaction between hydrazoic acid and the nitrous acidium ion, because Ridd found evidence for an acid catalysis of dinitrogen trioxide formation [1] (though the extent of the acid catalysis is less than in the present work).

The form of the rate equation, $v = k_3^{HN_3}[H^+][HNO_2][HN_3]$, is also consistent with a reaction between hydrazoic acid and an equilibrium concentration of nitrosonium ions:

$$H_2NO_2^+ \underset{\text{fast}}{\rightleftharpoons} NO^+ + H_2O \xrightarrow[\text{slow}]{HN_3} N_3{\cdot}NO + H_3O^+ \xrightarrow[\text{fast}]{} N_2 + N_2O + H_3O^+ \quad . \quad . \quad . \quad (11)$$

Hughes, Ingold, and Ridd have rejected mechanisms of this type in their studies of diazotisation,[1] by comparing their rates of reaction with the rate of oxygen exchange between nitrous acid and water.[3] Direct evidence from a study of the reaction between nitrous acid and hydrazoic acid in water enriched in oxygen-18 shows that chloride, bromide, and azide ions form the corresponding nitrosyl compounds by nucleophilic substitutions at the nitrous acidium ion and not at the nitrosonium ion.[7] It therefore seems very unlikely that the acid-catalysed reaction between nitrous acid and hydrazoic acid involves the nitrosonium ion.

These conclusions differ somewhat from those recorded by Seel *et al.*,[8] who suggest that nitrosyl azide is formed by reaction of hydrazoic acid, rather than azide ions, with a introsyl compound:

$$NO{\cdot}X + HN_3 \longrightarrow N_3{\cdot}NO + HX \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

The present work suggests that the alternative view is correct, *i.e.*, that nitrosyl compounds react with the azide ion and not with hydrazoic acid. The only exception observed is in the case of the highly reactive nitrous acidium ion.

Experimental

Materials.—Sodium azide was recrystallised from water and dried *in vacuo* over phosphorus pentoxide. "AnalaR" sodium nitrite was dried over phosphorus pentoxide. "AnalaR" perchloric acid, 60%, was used without further purification. All solutions were made up with boiled-out distilled water.

Kinetic Measurements.—The solutions containing sodium nitrite and sodium azide were made up in conical flasks and cooled to 0° in ice–water. Two initial samples were withdrawn for analysis. Reaction was started by adding the requisite quantity of ice-cold, concentrated

[8] Seel, Wölfle, and Zwarg, *Z. Naturforsch.*, 1958, **13***b*, 136.

perchloric acid (usually between 0·8 and 3·6M) from a pre-cooled pipette. Samples were withdrawn with an ice-jacketed pipette at suitable time intervals, and reaction was stopped by adding the sample to a known excess of concentrated sodium hydroxide solution. Care was taken to exclude carbon dioxide from all solutions, as sodium carbonate interfered with the analysis procedure.

Spectrophotometric Analysis.—Solutions were analysed by measuring the optical density at several wavelengths in the range 2450—2300 Å, a Unicam S.P. 600 with silica cells being used at fixed slit-widths. Beer's law was obeyed. Care was always taken to check that the ratios of the optical densities at several wavelengths did not change during the course of a run (with initially equal concentrations of azide and nitrite). This provided a check on the absence of side reactions, and the validity of the analytical method. Blanks were always run to check light absorption due to traces of carbonate in the solution.

The author of this and the following paper thanks Professor Sir Christopher Ingold, F.R.S., and Professor E. D. Hughes, F.R.S., for their interest and for helpful discussions. He is also indebted to Dr. C. A. Bunton and Dr. J. H. Ridd.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER STREET, LONDON, W.C.1.
[PRESENT ADDRESS: UNIVERSITY COLLEGE OF SWANSEA,
SINGLETON PARK, SWANSEA.]

[*Received, February 11th,* 1959.]

---

591. *Mechanism of the Azide–Nitrite Reaction. Part II.*[1]

By G. STEDMAN.

Reaction between nitrous acid and hydrazoic acid in the presence of a large excess of sodium azide–hydrazoic acid buffer at 0° occurred by a rate-determining nucleophilic attack by the azide ion on the nitrous acidium ion to form nitrosyl azide. This decomposed in a subsequent fast step to nitrogen and nitrous oxide. Added chloride, bromide, and thiocyanate ions catalysed the reaction, *via* the formation of the corresponding nitrosyl compounds. Each of these nitrosyl compounds was formed in a rate-determining step, and then reacted rapidly with the azide buffer to form nitrosyl azide, which then decomposed in a further fast step to nitrogen and nitrous oxide. Perchlorate and nitrate ions did not affect the rate of reaction, other than by a small salt effect. The relative nucleophilic reactivities of chloride, bromide, thiocyanate, and azide ions towards the nitrous acidium ion were 1 : 1·2 : 1·5 : 2·4. The results are compared with other investigations of the kinetics of reactions of nitrous acid and their significance is discussed.

IT has been shown[1] that there are two mechanisms whereby the azide–nitrite reaction occurred in the presence of excess of perchloric acid:

$$NO_2^- + H_2NO_2^+ \xrightarrow[\text{slow}]{} N_2O_3 + H_2O \xrightarrow[\text{fast}]{N_3^-} N_3{\cdot}NO + NO_2^- \xrightarrow[\text{fast}]{} N_2 + N_2O \quad . \quad . \quad . \quad (1)$$

$$HN_3 + H_2NO_2^+ \xrightarrow[\text{slow}]{} N_3{\cdot}NO + H_3O^+ \xrightarrow[\text{fast}]{} N_2 + N_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

No sign was found of a mechanism that might have been expected to occur, *viz.*, nucleophilic attack by the azide ion directly on the nitrous acidium ion to form nitrosyl azide, followed by decomposition to nitrogen and nitrous oxide:

$$N_3^- + H_2NO_2^+ \xrightarrow[\text{slow}]{} N_3{\cdot}NO + H_2O \xrightarrow[\text{fast}]{} N_2 + N_2O \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The reason is that the reactivities of various anions as nucleophilic reagents towards the nitrous acidium ion cover only a small range. Chloride, bromide, thiocyanate, iodide, and

[1] Stedman, Part I, preceding paper.

XUM

nitrite ions differ in reactivity by a factor of less than two.[2,3] It is, therefore, unlikely that the reactivity of the azide ion towards the nitrous acidium ion will be much greater. The dissociation constant of hydrazoic acid is about thirty-two times smaller than that of nitrous acid [4-6] at 0°. For equimolar amounts of the two acids, and in the presence of an appreciable excess of perchloric acid, the concentration of the azide ion will be thirty-two times lower than that of the nitrite ion. Hence the rate of reaction by (1) will be much greater than the rate of reaction by (3) in the region where $[H^+] < 0{\cdot}04$M. Above this acidity, reaction by mechanism (1) is unimportant,[1] but reaction by mechanism (2) becomes sufficiently important to give a much greater rate than (3). The present work was carried out with a large excess of sodium azide–hydrazoic acid buffer over nitrous acid. This ensured that $[N_3^-] \gg [NO_2^-]$, and hence that the rate of mechanism (3) > rate of mechanism (1). The low acidity of the buffer used, pH *ca.* 5, ensured that reaction by mechanism (2) was negligible.

Results.—Reaction was of first order in nitrite in all the runs carried out. All other species were present in a large and constant excess in any one run. The dependence of rate on acidity, concentration of added salts, ionic strength, etc., was found by comparing the first-order rate constants for various runs in which these quantities were varied. The results are given in Table 1.

TABLE 1. *Dependence of rate on azide buffer concentration and composition.*

Run No.	55	64	65	66	56
$10^2[HN_3]$ (M)	6·19	2·48	4·03	7·87	2·48
$10^2[N_3^-]$ (M)	3·81	7·52	5·73	2·29	1·52
$10^5[H^+]$ * (M)	1·65	0·334	0·71	3·47	1·65
10^5k_1 † (sec.$^{-1}$)	8·09	0·70	2·25	21·6	3·15
$10^{-6}k_1/[H^+]^2[N_3^-]$ (sec.$^{-1}$ mole^{-2} l.^{2})	7·80	8·35	7·79	7·84	7·63

* Calculated from $[H^+][N_3^-]/[HN_3] = 1{\cdot}0 \times 10^{-5}$ mole l.$^{-1}$ (Hantzsch, *Ber.*, 1899, **32**, 3073; Seel and Schwaebel, *Z. anorg. Chem.*, 1953, **274**, 169). † Corrected for ionisation of nitrous acid.

Buffer of Sodium Azide and Perchloric Acid.—The rate was proportional to the buffer concentration at constant composition, and the results fitted the rate equation $v = k[H^+]^2[NO_2^-][N_3^-]$ as can be seen from the last line of Table 1. This equation can be rearranged to the form $v = k_3^{N_3^-}[H^+][HNO_2][N_3^-]$, with $k_3^{N_3^-} = 2500$ sec.$^{-1}$ mole^{-2} l.^{2}. This rate equation is consistent with two possible mechanisms. One is a rate-determining nucleophilic attack by the azide ion on the nitrous acidium ion to form nitrosyl azide, as in mechanism (3). The other is a rate-determining reaction between azide ions and an equilibrium concentration of nitrosonium ions to form nitrosyl azide (4):

$$H_2NO_2^+ \underset{\text{fast}}{\rightleftharpoons} NO^+ + H_2O \xrightarrow[\text{slow}]{N_3^-} N_3{\cdot}NO \xrightarrow[\text{fast}]{} N_2 + N_2O \qquad \ldots\ (4)$$

These two possibilities cannot be distinguished on the basis of the evidence presented above. A distinction can be drawn by carrying out the reaction in water enriched in oxygen-18, and determining the isotopic composition of the evolved nitrous oxide. These experiments will be described in the later paper.[7] They show that isotopic abundance of the oxygen-18 tracer in the nitrous oxide is always much less than that of the water. This excludes the nitrosonium ion as a reaction intermediate. If reaction occurred as shown in equation (4) then nitrous acid would exchange oxygen atoms with water by the formation and rehydration of the nitrosonium ion much more rapidly than nitrous oxide was formed.

[2] Hughes, Ingold, and Ridd, *J.*, 1959, 58.
[3] Seel, Wölfle, and Zwarg, *Z. Naturforsch.*, 1958, **13***b*, 136.
[4] Seel and Schwaebel, *Z. anorg. Chem.*, 1953, **274**, 169.
[5] Klemmenc and Hayeck, *Monatsh.*, 1929, **54—55**, 407.
[6] Hantzsch, *Ber.*, 1899, **32**, 3073.
[7] Bunton and Stedman, *J.*, to be published.

XUM

Thus, nitrous acid would come into isotopic equilibrium with the solvent much more rapidly than reaction with azide ions occurred, and hence the isotopic composition of the evolved nitrous oxide would be the same as that of the solvent.

TABLE 2. *Effect of added salts on the rate of the azide–nitrite reaction at* 0°.

Run No.	55	56	60	62	58	61	59	63
[Buffer] (M)	0·10	0·04	0·04	0·08	0·04	0·08	0·04	0·08
Salt added	—	—	$NaNO_3$	$NaNO_3$	NaBr	NaBr	NaCl	NaCl
[Salt] (M)	—	—	0·06	0·06	0·06	0·06	0·06	0·06
10^5k_1 (sec.$^{-1}$)	8·1	3·2	3·6	7·7	10·6	14·5	9·1	14·0
$10^5(k_1 - k_1^*)$ ...	—	—	—	—	7·0	6·8	5·5	6·3

k_1^* is the value of k_1 for the same concentration of sodium nitrate, and at the same buffer concentration. For runs 58 and 59 $k_1^* = k_1$ for run 60. For runs 61 and 63 $k_1^* = k_1$ for run 62. $[HN_3]/[N_3^-] = 1{\cdot}63$ for all runs.

Hughes, Ingold, and Ridd [2] concluded that nitrosyl halides are formed in aqueous solution by nucleophilic attack of the halide ion on the nitrous acidium ion, and not on the nitrosonium ion. Their conclusion was based on a comparison of rates of diazotisation and oxygen exchange between nitrous acid and water, which were necessarily measured under very different conditions.[8] The present work provides direct support for their view; in this case the kinetic and isotopic results were obtained under very similar conditions.

Effect of Added Salts.—The effect of adding sodium perchlorate, nitrate, bromide, and chloride, and of potassium thiocyanate was investigated. The results are in Tables 2 and 3.

Buffer of Sodium Azide and Perchloric Acid.—The results in Table 2 show that sodium nitrate has only a small effect on the rate. This is what would be expected in view of its low nucleophilic power towards the nitrous acidium ion.[2,9] The small increase in rate due to addition of sodium nitrate is probably a salt effect.

Sodium bromide and sodium chloride produce much larger increases in rate. When the rate of uncatalysed reaction is subtracted from the total rate observed in the presence of bromide and chloride ions, the rate constant for the catalysed reaction alone is obtained. These values are in the fifth row of Table 2. (The rate of uncatalysed reaction has been taken as the rate observed for an equal concentration of added sodium nitrate, in order to allow for ionic strength effects.) It can be seen that for bromide ions the rate of catalysed reaction is independent of buffer concentration, while for chloride ions the rate of catalysed reaction is almost independent of buffer concentration. The bromide and chloride catalysis is due to a rate-determining formation of the corresponding nitrosyl compound, which reacts with azide buffer in a subsequent fast step to form nitrosyl azide which then decomposes to nitrogen and nitrous oxide:

$$Br^- + H_2NO_2^- \xrightarrow[\text{slow}]{} NO{\cdot}Br + H_2O \xrightarrow[\text{fast}]{\text{azide}} N_3{\cdot}NO + Br^- \xrightarrow[\text{fast}]{} N_2 + N_2O \quad . \; . \; . \quad (5)$$

It is not known whether the nitrosyl bromide reacts with azide ions or with hydrazoic acid. By analogy with dinitrogen trioxide,[1] one would expect the azide ion to be the reactive species. As, however, nitrosyl bromide is much more reactive than dinitrogen trioxide, hydrazoic acid may also act as a nucleophilic agent towards it. When the bromide- and chloride-catalysed reactions are carried out in water enriched in oxygen-18, the nitrous oxide evolved is only slightly isotopically enriched.[7] This again shows that reaction is not occurring between the nucleophilic anion and an equilibrium concentration of nitrosonium ions. A similar set of experiments to those summarised in Table 2 was carried out with use of a buffer of sodium azide and nitric acid. Nitric acid was used instead of perchloric acid because it was desired to study the effect of added potassium

[8] Bunton, Llewellyn, and Stedman, *J.*, in the press.
[9] Bunton, Halevi, and Llewellyn, *J.*, 1953, 2653; Stedman, Thesis, London, 1955.

thiocyanate on the rate of reaction, and this avoided difficulties due to the low solubility of potassium perchlorate. The results are given in Table 3.

TABLE 3. *Effect of added salts on the rate of the azide–nitrite reaction at 0°.*

Run No.	[Buffer] (M)	[Added salts]	10^5k_1 (sec.$^{-1}$)	$10^5(k_1 - k_1^*)$ (sec.$^{-1}$)
75	0·0615	—	5·7	—
79	0·0615	0·0615M-$NaNO_3$	6·3	—
80	0·0615	0·0615M-$NaClO_4$	6·1	—
76	0·0615	0·0615M-KNCS	16·6	10·4
84	0·0615	0·0615M-KNCS	16·5	10·3
77	0·0615	0·0615M-NaBr	14·1	7·9
78	0·0615	0·0308M-NaBr + 0·0308M-$NaClO_4$	10·3	4·1
83	0·0308	0·0923M-$NaClO_4$	3·2	—
85	0·0308	0·0308M-$NaClO_4$ + 0·0615M-KNCS	12·3	9·1
86 †	0·0615	0·0615M-$NaClO_4$	8·3	—
87 †	0·0615	—	7·6	—
82 †	0·0615	0·0615M-NaBr	13·3	—
90	0·117	—	12·1	—

k_1^* is the first-order rate constant observed for reaction when the catalysing salt, NaBr or KNCS, is replaced by an equal concentration of $NaNO_3$ or $NaClO_4$. For runs 76, 77, 78, and 84, k_1^* is the mean of k_1 for runs 79 and 80, *i.e.* $6·2 \times 10^{-5}$ sec.$^{-1}$. For run 85, k_1^* is k_1 for run 83, *i.e.* $3·2 \times 10^{-5}$ sec.$^{-1}$. In runs 82, 86, and 87, $[HN_3]/[N_3^-] = 2·23$. For all other runs $[HN_3]/[N_3^-] = 1·63$.

Comparison of runs 79 and 80 with run 75 shows that addition of 0·06M-sodium nitrate and sodium perchlorate has no large effect on the rate. There is a small increase in rate, *ca.* 10%, which is due to a salt effect. Addition of 0·06M-potassium thiocyanate produces a very much larger increase in rate. If the rate of the thiocyanate-catalysed reaction is obtained by subtracting from the value of k_1, for the total reaction, the value of k_1^*, for reaction in the presence of an equal concentration of added sodium perchlorate or nitrate, it is found that the rate of the thiocyanate-catalysed reaction is almost independent of buffer concentration. In runs 77 and 78 all factors were kept constant except the bromide-ion concentration, which was varied by a factor of two. The results in Table 3 show that the rate of the bromide-catalysed reaction is proportional to the bromide-ion concentration.

There is little doubt that the chloride, bromide, and thiocyanate catalysis of the azide–nitrite reaction is due to a rate-determining formation of the nitrosyl compound, followed by a rapid reaction with the azide buffer to give nitrosyl azide; this breaks down in a subsequent fast step to form nitrogen and nitrous oxide. This is shown in equation (5). The exact value of the rate constant for the nitrosyl compounds depends on the value taken for the dissociation constant of hydrazoic acid (in order to calculate the pH of the buffer), and the value of the dissociation constant of nitrous acid (in these buffers most of the nitrite is present as nitrite ion, whereas the value of $[HNO_2]$ is required for insertion into the rate equation). As most of these results were obtained in buffers of constant composition it is possible to obtain the relative nucleophilic reactivities of the various catalysing anions by dividing the rate constant for the catalysed reaction alone by the concentration of the catalysing anion. This gives the ratio

$$k_3^{Cl^-} : k_3^{Br^-} : k_3^{NCS^-} : k_3^{N_3^-} :: 1 : 1·2 : 1·5 : 2·4$$

These values are in good agreement with those obtained [2,8] from studies of diazotisation, $k_3^{Br^-} : k_3^{NCS^-} :: 1·2 : 1·55$. The actual values of the rate constants are $k_3^{Br^-} = 1250$ sec.$^{-1}$ mole^{-2} l.^{2} and $k_3^{NCS^-} = 1560$ sec.$^{-1}$ mole^{-2} l.^{2}, and these are in good agreement with the values obtained [2,8] from diazotisation, 1170 and 1500 sec.$^{-1}$ mole^2 l.$^{-2}$, respectively. One should not attach too much significance to the numerical agreement, because the rate constants obtained in the present work depend for their absolute values on the square of the dissociation constant of hydrazoic acid, and on the reciprocal of the dissociation constant of nitrous acid. These dissociation constants are subject to considerable possible error, and hence the absolute values of the rate constants are also subject to this error.

The relative values should be unaffected. If the relative reactivities of chloride, bromide, thiocyanate, and azide ions are taken as accurate, and if the value for $k_3^{Br^-}$ is taken [2] as 1170 sec.$^{-1}$ mole^{-2} l.^{2}, then the values of $k_3^{Cl^-}$, $k_3^{NCS^-}$, and $k_3^{N_3^-}$ are 975, 1460, and 2340 sec.$^{-1}$ mole^{-2} l.^{2} at 0°.

The small difference in nucleophilic reactivity of the azide and chloride ions furnishes strong evidence for the high reactivity and low selectivity of the nitrous acidium ion and it would seem that the breaking of the nitrogen–oxygen bond is much more important than the formation of the new bond with the incoming nucleophilic reagent. The very low reactivity of the nitrate ion may be due to there being no free lone pair of electrons on the nitrogen atom, the p electrons forming a double bond with the more electronegative oxygen atoms, and resonating among the three possible positions.

The value of $k_3^{Cl^-}$ is of some interest, as kinetic investigations of the mechanism of diazotisation were not able to provide data on the rate of substitution of this ion at the nitrous acidium ion to form nitrosyl chloride. Previous work had shown that chloride ions had a much lower catalytic effect on the rate of diazotisation than had an equal concentration of bromide ions. The present results show that this is not due to a much lower rate of formation of nitrosyl chloride than of nitrosyl bromide, and that the different catalytic effects must be due to different ratios of the reactivity of the nitrosyl halides towards water and the amine being diazotised. The results are in interesting contrast to those of Allen,[10] who studied the halide-catalysed hydrolysis of alkyl nitrites in aqueous dioxan. He found that for reaction (6):

$$X^- + Pr^nO{\cdot}N{\cdot}OH^+ \longrightarrow NO{\cdot}X + Pr^nOH + H^+ \ (X = Cl \text{ or } Br) \quad . \ . \ . \ . \ . \quad (6)$$

the relative reactivities of chloride and bromide ions were 1 : 0·7. Bunton and Masui [11] studied the same reaction in water, and found that the relative reactivities are chloride ion : bromide ion :: 1 : 1·2, as in the present work. The reason for this reversal in relative reactivities between water and aqueous dioxan is not clear.

Seel and his co-workers [3] have studied the effect of adding salts on the rate of the azide–nitrite reaction.[4] Their results for chloride and bromide are in agreement with those of the present work, but they claim that the nitrate ion has a nucleophilic reactivity of one half that of the bromide ion. This is at variance with Abel's work on the decomposition of nitrous acid,[12] and with the present work. The discrepancy may be due to the fact that Seel and his co-workers worked at an ionic strength of 1·2M where specific salt effects may vary by amounts similar to the small differences in nucleophilic reactivity of various anions.

Experimental

Materials.—The materials used were the same as those described in the previous paper.[1]

Kinetic Measurements.—The procedure was similar to that described earlier,[1] except that reaction was started by adding ice-cold sodium nitrite solution to the cooled azide buffer, instead of acidifying an azide–nitrite solution. Reaction was stopped by adding the sample to an excess of concentrated sodium hydroxide solution, and the amount of reaction determined by measuring the light absorption due to the nitrite ion, at 3520 Å, a Unicam spectrophotometer with 4-cm. silica cells being used. A slight background absorption due to the nitrate ion was corrected for by use of a blank solution.

Calculations.—In order to calculate the values of the rate constants $k_3^{N_3^-}$, $k_2^{Br^-}$, etc., it is necessary to know the values of $[H^+]$ and of $[HNO_2]$. The values of $[H^+]$ were calculated from the known composition of the buffer, and from the value for the dissociation constant of hydrazoic acid of $1{\cdot}0 \times 10^{-5}$M at 0°. This is an old value due to Hantzsch [6] but is believed to be reliable. Hantzsch measured the dissociation constants conductometrically and obtained values of $1{\cdot}0 \times 10^{-5}$ at 0° and $1{\cdot}9 \times 10^{-5}$ at 25°. The latter is in good agreement with the

[10] Allen, *J.*, 1954, 1968.
[11] Bunton and Masui, personal communication.
[12] Bray, *Chem. Rev.*, 1932, **10**, 161.

modern values $2{\cdot}04 \times 10^{-5}$ at 25° (ref. 4), and $2{\cdot}1$, $2{\cdot}2$, and $1{\cdot}9 \times 10^{-5}$ at 25° (ref. 13). West [14] obtained a value $1{\cdot}7 \times 10^{-5}$ at 25°, again conductometrically, and Hantzsch's value at 0° can be compared with another conductometric value at 0°, $0{\cdot}8 \times 10^{-5}$, due to Oliveri-Mandala'.[15]

These results underline the reliability of the value of $1{\cdot}0 \times 10^{-5}$ for the dissociation constant of hydrazoic acid at 0°, even though it is an early one. It is important to establish this value, as it is desirable to compare the values of $k_3^{Br^-}$ and $k_3^{NCS^-}$ obtained in this work with those obtained in other investigations.

First-order rate constants, k_1, were obtained from the slopes of conventional plots of $\log_{10}$ [nitrite] against time.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER STREET, LONDON, W.C.1.
[PRESENT ADDRESS: UNIVERSITY COLLEGE OF SWANSEA,
SINGLETON PARK, SWANSEA.]

[*Received, February 11th*, 1959.]

[13] Tui, *Bull. Inst. Phys. Chem. Res., Tokyo*, 1941, **20**, 390.
[14] West, *J.*, 1900, 705.
[15] Oliveri-Mandala', *Gazzetta*, 1916, **46**, I, 298.

---

592. *Chemical Applications of Nuclear Quadrupole Resonance Spectroscopy. Part III.*[1,2] *The Inductive Effect of Substituents belonging to the First Row of the Periodic Table.*

By E. A. C. LUCKEN.

Nuclear quadrupole resonance spectra of chloro-derivatives of a number of aliphatic ethers, sulphides, fluoro-, allyl, and propargyl compounds, have been measured with a frequency-modulated, externally quenched, super-regenerative spectrometer. The anomalously low frequencies of the compounds containing fluorine and oxygen substituents have been interpreted in terms of overlap between the *p*-orbitals of the first-row substituent and the carbon–chlorine σ-bond. A molecular-orbital treatment of the effect is given in an Appendix. In allyl and propargyl compounds little or no anomaly occurs.

PREVIOUS Parts [1,2] in this series have been primarily concerned with the effects of conjugation on nuclear quadrupole resonance frequencies of ^{35}Cl. In this paper is discussed the effect of the first-row substituents fluorine and methoxyl in the α-position to the chlorine nucleus under investigation. It was first observed by Livingstone [3] that the nuclear quadrupole resonance frequencies of ^{35}Cl of the chlorofluoromethanes were anomalously low, and in an attempt to confirm and explain this anomaly for similar α-fluoro-substituted aliphatic compounds and the related α-chloro-ethers this investigation has been carried out.

Experimental.—The ^{35}Cl resonances were detected by the method described in Part I.[1] Propargyl chloride [4] and 2-chloroethyl methyl ether [5] were prepared by standard methods, and the latter was fractionated before use. A commercial specimen of chloromethyl methyl ether was dried and fractionated, and specimens of chloromethyl methyl sulphide, bischloromethyl sulphide, 2,2′-dichlorodiethyl ether, allyl chloride, and methallyl chloride were distilled before use. The remaining commercial specimens were used without further purification. 2,2-Dichloro-1,1,1-trifluoroethane was a gift from Imperial Chemical Industries Limited. The observed frequencies are shown in Table 1.

[1] Part I, Dewar and Lucken, *J.*, 1958, 2653.
[2] Part II, Dewar and Lucken, *J.*, 1959, 426.
[3] Livingstone, *J. Phys. Chem.*, 1953, **57**, 496.
[4] Hatch and Chiola, *J. Amer. Chem. Soc.*, 1951, **73**, 360.
[5] Swatten and Boord, *ibid.*, 1930, **52**, 651.

TABLE 1. *Nuclear quadrupole resonance frequencies of* ^{35}Cl, *at 77° K unless otherwise stated, in Mc. per sec.*

Chlorodimethyl ether	30·181	1,1,3,3-Tetrachloro-1,3-difluoro-acetone	39·312 39·104
2-Chloroethyl methyl ether	33·453	2,3-Dichloro-1,1,1,4,4,4-hexafluoro-but-2-ene	39·491
2,2′-Dichlorodiethyl ether	33·392 33·483	1,2-Dichloro-3,3,4,4,5,5-hexafluoro-cyclopentene	38·039
Chlorodimethyl sulphide	33·104	1,1-Dichloro-2,2,2-trifluoroethane	38·694
2,2′-Dichlorodimethyl sulphide	34·749 34·526	Allyl chloride	33·398 (86° K)
Dichlorofluoroacetic acid	39·594	Methallyl chloride	33·777
Chlorodifluoroacetic acid	37·485	Propargyl chloride	35·753 (86° K)

DISCUSSION

The frequencies of the chlorofluoroacetic acids are both lower than those of trichloroacetic acid (39·96, 40·165, 40·240 Mc./sec. at 77° K), the frequency decreasing with an increasing degree of substitution by fluorine. This trend is similar to that noted by Livingstone in the chlorofluoromethanes, and the effect on the chlorine-resonance frequency of a fluorine atom in a position α to the chlorine atom may thus be said to be established.

In order to explain the anomalously low ^{35}Cl nuclear quadrupole resonance frequencies of the chlorofluoromethanes it was suggested that in those compounds the carbon–chlorine bond is endowed with some π-character by hyperconjugation of form (II). Moderate amounts of such double-bond character can be shown to lower the resonance frequency. Since a structure such as (II) involves a positive charge on the chlorine atom, it is supposed to be favoured by the high electronegativity of fluorine.

(I) (II)

Although it is probable that such carbon–chlorine double-bonding does occur in saturated molecules, the effect is likely to be small. Even when the chlorine atom is attached to an unsaturated residue, *e.g.*, vinyl chloride, it has been shown by measurements of the nuclear quadrupole resonance asymmetry parameter that the carbon–chlorine bond has only 5—15% of π-character. In any case, according to the above hypothesis the amount of π-character in the carbon–chlorine bond will be proportional to the electronegativity of the substituents, and thus its effect on the nuclear quadrupole resonance frequency of chlorine could not be separated from that due to inductive polarisation. There is thus no reason why the effect of fluorine substituents should be anomalous.

An alternative explanation was suggested by the frequency of bischloromethyl ether. It is well known that elements in the first row of the Periodic Table are particularly suited to the formation of π-bonds by the overlap of *p*-orbitals. This effect, in the case of fluorine, is well illustrated by the acid and base dissociation constants of the *para*-halogeno-phenols and -anilines respectively (Table 2),[6] where the expectedly high inductive effect of the

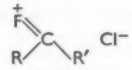
TABLE 2. *Acid* ($K_A \times 10^{11}$) *and base* ($K_B \times 10^{12}$) *dissociation constants of para-halogenophenols and -amines.*

X =	F	Cl	Br	I	H
p-X·C_6H_4·OH	2·6	13·2	15·5	21·9	3·2
p-X·C_6H_4·NH_2	120	28·8	21·9	15·1	12·6

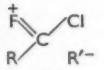
fluorine atom is offset by its ability to conjugate with the benzene ring. In view of the above a structure such as (III) may contribute significantly to the ground state of chlorofluoromethane or a related molecule. This would increase the ionic character of the carbon–chlorine bond and so lower the nuclear quadrupole resonance frequency of chlorine.

[6] Sharpe and Haszeldine, "Fluorine and its Compounds," Methuen, London, 1951.

The type of interaction invoked is essentially similar to the previous one but it is immediately obvious why fluorine should be different from chlorine, for its ability to form double bonds is so much greater.



(III)



(IV)

The problem has so far been discussed in valence-bond terms which here have the advantage of pictorial clarity and permit a ready comparison with the previous explanation of the anomaly. A molecular-orbital discussion is equally possible and in this case enables an estimate of the magnitude of the effect to be obtained in a straightforward manner. A calculation along these lines has been carried out in the Appendix and it is shown that the magnitude of the interaction between the substituent p-orbital and the

FIG. 1.

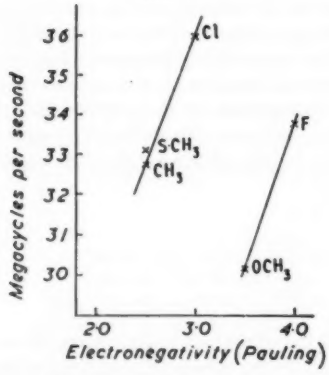
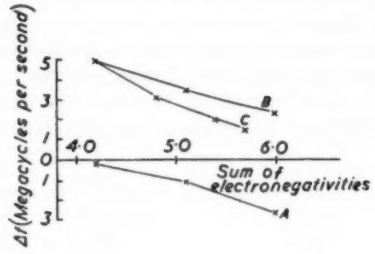


FIG. 2



carbon–chlorine σ-bond is quite sufficient to account for the observed reduction in frequency.

From this hypothesis we may draw a number of conclusions. First, that the chlorine nuclear quadrupole resonance frequencies of molecules XRR'CCl will also be anomalously low when X is RO or RR'N. Secondly, that the frequencies of these molecules will be in the order $X = F > OMe > NMe_2$. Thirdly, that if either of the substituents R,R' is appreciably electronegative then the effect of the postulated hyperconjugation on the chlorine frequency will be reduced since structures such as (IV) will also contribute to the ground state of the molecule

Fig. 1 has been constructed by plotting the chlorine nuclear quadrupole resonance frequency of the molecule $R{\cdot}CH_2Cl$, where R is an atom or radical, against the electronegativity of the atom in R directly attached to the carbon atom. It illustrates the correctness of the first two conclusions. The points corresponding to chlorofluoromethane and chlorodimethyl ether lie at a much lower frequency than those corresponding to molecules in which hyperconjugation is not expected to occur. The results are sparse, but there is no doubt that the frequency of chlorodimethyl ether is much lower than would have been expected on the grounds of a simple inductive effect. It is possible, though with perhaps little justification, to draw two roughly parallel lines through the points on the Figure, one through those in which hyperconjugation occurs and one through those in which it does not. The parallelism, if real, implies that the reduction in frequency due to hyperconjugation is the same in chlorofluoromethane as in chlorodimethyl ether and hence that the amount of π-character in the carbon–fluorine bond is approximately the same as that in the carbon–oxygen bond. If the lower of these two lines is produced to

cut the electronegativity axis at 3·0, corresponding to a NMe_2 substituent, a frequency of approximately 27 Mc./sec. is predicted for the molecule $NMe_2{\cdot}CH_2Cl$, corresponding to a highly polar carbon–chlorine bond. Such a molecule would be very reactive and this could account for the lack of success in attempts to prepare α-chloro-amines.

TABLE 3. ^{35}Cl *Nuclear quadrupole resonance frequencies of chlorofluoromethanes at* 20° K.

R	R′	(f_1) RR′CHCl	(f_2) RR′CCl_2	(f_3) RR′CFCl	$f_1 - f_3$	$f_2 - f_3$
H	H	68·40	72·47	67·6	+0·8	+4·9
H	Cl	72·47	76·98	73·53	−1·06	+3·45
Cl	Cl	76·98	81·85	79·63	−2·65	+2·22

The correctness of the third conclusion may be illustrated by reference to the frequencies of the chlorofluoromethanes. In Table 3 are shown the chlorine nuclear quadrupole resonance frequencies of the molecules RR′CHCl, RR′CFCl, and RR′CCl_2, and the frequency differences between the pairs RR′CFCl–RR′CHCl and RR′CCl_2–RR′CFCl. In Fig. 2 these differences are plotted against the sum of the electronegativities of R and R′. It is seen that, as expected, two parallel lines are obtained, one (*A*) for substitution of hydrogen by fluorine, and the other (*B*) for the substitution of chlorine by fluorine.

The evidence for the present hypothesis, although far from conclusive, is thus strong enough to justify its use as a basis for discussion. Reference to Fig. 1 shows that the effect of this hyperconjugation is to reduce the effective electronegativity of the first-row substituent by approximately 1·3 electronegativity units. The frequency of 2-chloroethyl methyl ether is thus comparable with that of n-propyl chloride (33·0 Mc./sec.), while that of 1,1-dichloro-2,2,2-trifluoroethane is close to that of pentachloroethane. The frequencies of 2,3-dichloro-1,1,1,4,4,4-hexafluorobut-2-ene and 1,2-dichloro-3,3,4,4,5,5-hexafluorocyclopentadiene are likewise consistent with this.

In Fig. 2 are also plotted points (line *C*) corresponding to line *B*, for which at least one of the substituents R, R′ is a fluorine atom. The electronegativity of fluorine is taken as 2·7 in accordance with the conclusions of the preceding paragraph, and it is seen that the trend is very similar to that shown in lines *A* and *B*. It must be emphasised, however, that this effective electronegativity of fluorine is not a constant but will depend very much on its molecular environment.

The interaction invoked may also be used to explain the observed bond-shortening in the chlorofluoromethanes. The statement that the hyperconjugation appears to reduce the electronegativity of the fluorine atom can be re-expressed by saying that hyperconjugation appears to increase the electronegativity of the chlorine atom. If we assume, by extrapolation of the upper line in Fig. 1, that the expected frequency of chlorofluoromethane is about 42 Mc./sec., then the lowering is 8 Mc./sec. Making use of the approximate relationship [7] between the electronegativity difference and quadrupole resonance frequency of diatomic molecules, *viz.*,

$$\text{Electronegativity difference} = 2\left\{\frac{\text{Observed frequency}}{\text{Atomic coupling frequency}}\right\}$$

we find that the change in electronegativity of the chlorine atom is approximately 0·3 electronegativity unit. From the Schomaker–Stevenson rule [8] this would produce a shortening in the carbon–chlorine bond length of $0{\cdot}09 \times 0{\cdot}3 = 0{\cdot}027$ Å. The observed difference in the carbon–chlorine bond lengths between methyl chloride and chlorofluoromethane is $0{\cdot}015 \pm 0{\cdot}007$ Å. Although this calculation is far from exact, particularly in view of the uncertainty in the mutual relation of atomic and bond parameters, it gives an answer of the correct magnitude.

The frequencies of the two sulphides accord with the accepted electronegativity of sulphur (2·5) and thus may be said to support the contention in Part II [2] that the high

[7] Gordy, Smith, and Tramburolo, "Microwave Spectroscopy," Wiley, 1953.
[8] Schomaker and Stevenson, *J. Amer. Chem. Soc.*, 1941, **63**, 37.

chlorine nuclear quadrupole resonance frequencies of the chlorothiophens are due to sulphur's use of *d*-orbitals in these compounds.

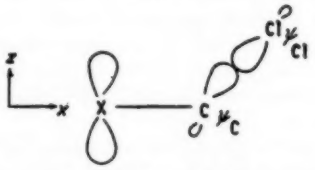
For allyl and propargyl chloride the frequencies are consistent with the assumption that vinyl and ethynyl groups act only as electronegative inductive substituents. From Fig. 1 we may calculate the electronegativity of the sp^2-carbon atom as 2·7 and of the *sp*-carbon atom as 2·9. These values are in accord with other independent estimates.[7] Although at first sight the situation in these compounds is analogous to that in fluoro- and methoxy-compounds, it is in fact fundamentally different. The important point is that, whereas the latter compounds form an odd conjugated system, the former form an even system. There is considerable evidence [9] which suggests that conjugation in even systems is very much less important than in odd ones and, if this is the case, it would probably be impossible to detect hyperconjugation in allyl and propargyl chlorides. It is hoped to discuss this question in more detail in a subsequent paper.

Appendix

Molecular-orbital treatment of the interaction between an α-substituent p-*orbital and the carbon–chlorine σ-bond.*

The following discussion is not intended to be rigorous; it does, however, show that the observed magnitude of the anomaly is consistent with the interaction invoked.

Fig. 3.



Chlorine nuclear resonance experiments show that an average aliphatic carbon–chlorine bond has about 35% of ionic character. In a simple L.C.A.O. treatment of a single bond, with neglect of overlap, this is consistent with a coulomb integral for chlorine of $\alpha_C + \beta$, where α_C is the carbon coulomb integral and β is the carbon–chlorine resonance integral. With these values for the parameters involved, the linear combination of atomic orbitals treatment of the carbon–chlorine single bond gives

$$\Psi_{\text{bonding}} = 0{\cdot}526\psi_C + 0{\cdot}850\psi_{Cl}$$
$$\Psi_{\text{antibonding}} = 0{\cdot}850\psi_C - 0{\cdot}526\psi_{Cl}$$

where ψ_C and ψ_{Cl} are the appropriate atomic orbitals for carbon and chlorine respectively.

It is convenient to assume that the substituent *p*-orbital interacts only with the empty antibonding orbital. This method has been used with success to explain the effect of substituents on the ultraviolet spectrum of benzene.

It is next required to determine the matrix elements of the second-order secular determinant describing the interaction. Let

$$\chi_1 \equiv \Psi_{\text{antibonding}}$$
$$\chi_2 \equiv \text{the substituent } p\text{-orbital}$$

then
$$\int \chi_1 H \chi_1^* d\tau \equiv H_{11} = \alpha_C - 0{\cdot}618\beta$$

and let
$$\int \chi_2 H \chi_2^* d\tau \equiv H_{22} = \alpha_C + b\beta$$

where *b* is a parameter which depends on the electronegativity of the substituent and will have values between 0 and 2, and

$$\int \chi_1 H \chi_2^* d\tau = \int \chi_2 H \chi_1^* d\tau \equiv H_{12} = x\beta$$

[9] Dewar and Schmeising, *Tetrahedron*, 1959, **5**, 166.

where x is a parameter depending on the amount of interaction between the substituent p-orbital and the antibonding carbon–chlorine molecular orbital.

An order of magnitude of x may be obtained from the following considerations. In Fig. 3 the orbitals in question are shown against a set of axes. All three atoms lie in the plane of the paper and χ_2 is a p_z-orbital. Then

$$\int \chi_2 H \chi_1 d\tau \equiv 0{\cdot}850 \int \chi_2 H \psi_C d\tau - 0{\cdot}526 \int \chi_2 H \psi_{Cl} d\tau$$

We may reasonably put $$\int \chi_2 H \psi_{Cl} d\tau = 0$$

Now $$\psi_C = \frac{1}{2}s + \frac{\sqrt{3}}{2}\left(\frac{1}{3}p_x + \frac{2\sqrt{2}}{3}p_z\right)$$

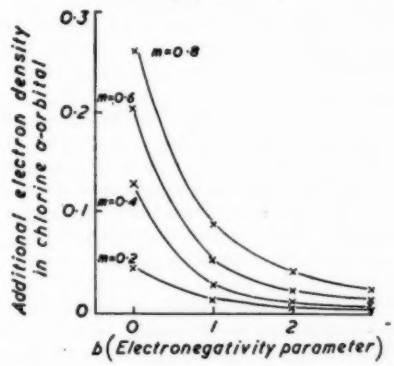
where s, p_x, p_z, are the $2s$, $2p_x$, and $2p_z$ orbitals of carbon. Thus

$$\int \chi_2 H \psi_C d\tau = \frac{1}{2}\int \chi_2 H s d\tau + \frac{\sqrt{3}}{2}\left[\frac{1}{3}\int \chi_2 H p_x d\tau + \frac{2\sqrt{2}}{3}\int \chi_2 H p_z d\tau\right]$$

From the symmetry properties of s and p_x orbitals it is evident that the first two integrals on the right-hand side are equal to zero. Thus

$$\int \chi_2 H \chi_1 d\tau = 0{\cdot}850 \sqrt{\frac{2}{3}} \int \chi_2 H p_z d\tau \simeq 0{\cdot}7 \int \chi_2 H p_z \, d\tau$$

FIG. 4.



Now, in general, $\int \chi_2 H p_z d\tau$ will be less than β, the carbon–chlorine resonance integral; *i.e.*, the ratio

$$\int \chi_2 H p_z d\tau / \beta \equiv m$$

will probably be less than unity. The secular determinant is thus:

$$\begin{vmatrix} \alpha + b\beta - E & 0{\cdot}7m\beta \\ 0{\cdot}7m\beta & \alpha - 0{\cdot}618\beta - E \end{vmatrix} = 0$$

Putting $A = (\alpha - E)/\beta$, we may expand this to give

$$A^2 + A(b - 0{\cdot}618) - (0{\cdot}49m^2 + 0{\cdot}618b) = 0$$

The electron density in the chlorine σ-orbital may then be obtained from the roots of this equation.

In Fig. 4 are plotted curves relating the electron density in the chlorine σ-orbital to the electronegativity of the substituent for various values of m. If it is remembered that 0·1 on

the electron-density scale corresponds to a decrease of approximately 5·5 Mc./sec., it can be seen that the interaction is of the right order. In view of the approximation that interaction is only with the antibonding orbital, it is likely that the above analysis will underestimate the frequency-lowering. Qualitatively, it can be seen that it is very sensitive to the choice of the electronegativity and resonance integrals. Resonance integrals are functions of bond length, and since the carbon–fluorine bond length (1·33 Å) is less than the carbon–oxygen bond length (1·42 Å), this would account for the observed equality of the hyperconjugative interaction in the fluoro- and methoxy-compounds.

The author thanks the Central Research Fund of the University of London for a grant for apparatus, and Professor M. J. S. Dewar for his interest and helpful discussion.

QUEEN MARY COLLEGE, MILE END ROAD, LONDON, E.1. [*Received, March 16th*, 1959.]

---

593. *Magnetic Studies with Copper(II) Salts. Part V.*[1] *Binuclear Derivatives of Copper(II) Formate involving Covalent Copper-to-Copper δ-Bonds.*

By R. L. MARTIN and HANNEKE WATERMAN.

The preparation of five novel derivatives of copper formate is described. They are the emerald-green heterocyclic monoamine copper(II) formates, $Cu(H{\cdot}CO_2)_2$,amine, where amine = pyridine, α-, β-, or γ-picoline, and the blue-green hemidioxan derivative, $Cu(H{\cdot}CO_2)_2,\frac{1}{2}C_4H_8O_2$. They provide the first examples in which copper formate has been " conditioned " into adopting the binuclear copper acetate-type structure, and their magnetic properties are remarkable, being zero below *ca.* 120° K, but rising to $\mu \simeq 1{\cdot}2$ B.M. at the decomposition temperature (*ca.* 360° K).

The anomalous temperature-variation of their magnetic susceptibilities provides strong evidence for their binuclear structures. The energy separation between singlet and triplet states, which arise from intramolecular exchange between pairs of contiguous copper atoms, is found to be twice that previously observed for anhydrous and hydrated copper(II) n-alkanoates (*J ca.* 600 cm.$^{-1}$ compared with 309 cm.$^{-1}$). This reflects an increase in binding energy of the postulated copper-to-copper covalent δ-bond in these compounds.

The compounds provide a unique opportunity for measuring directly the small temperature-independent contribution from copper to the paramagnetic susceptibility. Values for the four heterocyclic amine derivatives fall in the range, $N\alpha = 168\ (\pm 10) \times 10^{-6}$, while for the hemidioxan derivative a slightly smaller value, $N_\alpha = 128 \times 10^{-6}$, is observed.

The influence of both the amines and dioxan in " conditioning " copper formate so that it adopts the binuclear configuration is discussed.

COPPER(II) FORMATE displays[1] a marked reluctance to adopt the binuclear copper(II) acetate-type structure[2] (I) (p. 2966), which characterizes the cupric salts of the heavier homologues in the series of n-alkanoic acids. However, although anhydrous or hydrated binuclear copper(II) formate could not be isolated, strong evidence for the ephemeral existence of the binuclear species $[Cu_2(H{\cdot}CO_2)_4,L_2]$, where L is probably formic acid, water, or acetone, was provided by the absorption spectra in solution. These solutions exhibit an extra absorption band at 3700 Å which is not normally observed in the spectra of copper(II) compounds, but characterizes the spectra of the heavier binuclear copper(II) alkanoates. The blue-green solution obtained by dissolving copper carbonate in a mixture of formic acid and dioxan also exhibited this band at 3750 Å, but in this case dichroic blue-

[1] Part IV, Martin and Waterman, *J.*, 1959, 1359.
[2] Bleaney and Bowers, *Proc. Roy. Soc.*, 1952, *A*, **214**, 451.

green crystals of copper formate containing dioxan could be isolated from solution. The magnetic moment, measured at room temperature, of the crystals,[3] $\mu \sim 1$ B.M., was considerably lower than the corresponding values for heavier copper n-alkanoates,[4] $\mu =$ 1·38 B.M., or for the other modifications of copper formate which lie in the range, $\mu =$ 1·59—1·93 B.M.[1]

The binuclear structure (I), in which the two copper atoms are virtually contiguous [Cu–Cu = 2·64 Å in copper(II) acetate monohydrate] will be energetically unstable if a large residual electrostatic charge, of either sign, remains on the copper atoms after bonding to formate groups has taken place. Accordingly, the observed reluctance of anhydrous or hydrated copper formate to adopt this structure may well arise from the comparatively low σ-electron density on formate oxygen atoms, leading to a relatively large residue of positive charge on each copper atom after formation of the compound. If this is, in fact, the case, it should be possible considerably to reduce this excess of positive charge, and so favour structure (I) by forming a dative bond to copper in the terminal positions, L, by using a ligand of appropriate σ-electron charge density.

This hypothesis has now been tested with the ligands L = pyridine, α-, β-, and γ-picoline, aniline, and dioxan, and the experiments now described have led to the isolation and characterization of hitherto unknown binuclear derivatives of copper formate.

Experimental

Materials.—Copper formate–hemidioxan. Treatment of copper carbonate with a mixture of 98% formic acid and dioxan (1 : 2 v/v) yielded a dark green solution from which very small, dark dichroic blue-green rods of the hemidioxan derivative immediately crystallised. When reaction was complete, the crystals were washed and rapidly transferred to a desiccator, in which the adhering dioxan was removed at reduced pressure over calcium chloride. Although the *compound* was decomposed by moisture in the air, it was stable *in vacuo* at 150° (Found: C, 24·1; H, 2·85; Cu, 32·0. $CuC_4H_6O_5$ requires C, 24·3; H, 3·1; Cu, 32·2%); m. p. 190—200° (decomp.). A monodioxan compound could not be prepared.

Copper formate derivatives with amines. When anhydrous copper formate was dissolved at 70° in the appropriate freshly-distilled amine, a deep royal-blue solution was obtained. Slow evaporation at room temperature yielded royal-blue or violet crystals of the bisamine derivatives. When these were left for several days at reduced pressure over concentrated sulphuric acid, they lost one molecule of amine to form the corresponding emerald-green copper formate monoamine derivatives. The latter were insoluble in all non-donor solvents, and in acetone and alcohol, but very slightly soluble in dioxan. In water the complexes were destroyed, and in the appropriate amine, the tetrakisamine cupric complex was formed. The m. p.s of small quantities of the materials could be determined in capillary tubes, melting in each case being accompanied by loss of amine and reduction to copper. Surprisingly, the larger amounts contained in the Gouy tube during magnetic measurements decomposed rapidly at temperatures considerably below the m. p.

Copper formate–pyridine, m. p. 144° (Found: C, 36·0; H, 3·1; N, 6·2; Cu, 27·1. $C_7H_7O_4NCu$ requires C, 36·1; H, 3·0; N, 6·0; Cu, 27·3%). *Copper formate–α-picoline*, m. p. 135° (Found: C, 38·6; H, 3·7; N, 5·7; Cu, 25·5. $C_8H_9O_4NCu$ requires C, 39·0; H, 3·7; N, 5·7; Cu, 25·8%). *Copper formate–β-picoline*, m. p. 128° (Found: C, 38·8; H, 3·6; N, 5·55; Cu, 25·3%). *Copper formate–γ-picoline*, m. p. 126° (Found: C, 38·5; H, 3·8; N, 5·8; Cu, 25·4%). *Copper formate–bisaniline* separated as golden leaflets when benzene was added to a solution of copper formate in freshly distilled aniline at 70°. Attempts to transform the product into the monoaniline derivative were unsuccessful (Found: C, 49·2; H, 4·6; N, 8·3; Cu, 18·5. $C_{14}H_{16}O_4N_2Cu$ requires C, 49·5; H, 4·8; N, 8·2; Cu, 18·7%); m. p. 114° (decomp. at 120°).

Copper acetate derivatives of dioxan. Copper acetate–hemidioxan was prepared in hot solution by the method used for the corresponding formate. It so readily lost dioxan that complete analysis could not be carried out (Found: Cu, 28·8. $C_6H_{10}O_5Cu$ requires Cu, 28·2%). The hot mother-liquor from this preparation yielded large blue crystals of the *monodioxan derivative* on cooling. This was more stable than the hemidioxan compound, although it too decomposed on

[3] Martin and Whitley, *J.*, 1958, 1394.
[4] Martin and Waterman, *J.*, 1957, 2545.

TABLE 1. *Experimental gram and molar susceptibilities (c.g.s., e.m.u.) and magnetic moments (B.M.) at various absolute temperatures.*

Copper formate–bisaniline

Temp. (°K)	$10^6\chi_g$	$10^6\chi_M$ *	μ (B.M.) *
100·5	12·2	4318	1·86
109·7	11·1	3943	1·85
124·6	9·78	3495	1·86
152·2	7·83	2833	1·85
173·7	6·59	2412	1·82
201·5	5·73	2119	1·83
247·9	4·65	1753	1·84
273·5	4·18	1592	1·84
295·7	3·87	1487	1·84
318·7	3·57	1386	1·85
342·5	3·30	1293	1·85
358·0	3·10	1226	1·84

* Diamagnetic correction, $10^6\Delta = -172$; $N\alpha = 60 \times 10^{-6}$.

Copper formate–pyridine

Temp. (°K)	$10^6\chi_g$	$10^6\chi_M$ †	μ (B.M.) ($N\alpha = 60 \times 10^{-6}$)	μ (B.M.) ($N\alpha = 168 \times 10^{-6}$)
85·9	0·258	156	0·255	0
92·8	0·275	160	0·274	0
100·0	0·264	157	0·280	0
116·0	0·254	155	0·298	0
138·0	0·333	173	0·355	0·075
166·1	0·653	248	0·502	0·327
194·5	0·935	314	0·631	0·479
226·5	1·24	385	0·770	0·630
257·6	1·54	454	0·905	0·771
295·0	1·78	510	1·04	0·902
325·0	1·95	550	1·13	1·00
351·0	2·01	564	1·20	1·06
359·5	2·03	568	1·21	1·07
370·3	2·01	564	1·23	1·09

† Diamagnetic correction, $10^6\Delta = -96$.

Copper formate–α-picoline

Temp. (°K)	$10^6\chi_g$	$10^6\chi_M$ *	μ (B.M.) ($N\alpha = 60 \times 10^{-6}$)	μ (B.M.) ($N\alpha = 168 \times 10^{-6}$)
84·3	0·278	177	0·282	0
89·0	0·274	176	0·289	0
95·0	0·238	167	0·286	0
101·4	0·238	167	0·296	0
107·0	0·235	166	0·303	0
118·4	0·227	164	0·315	0
128·5	0·246	169	0·336	0
144·5	0·326	188	0·386	0·153
170·0	0·544	242	0·500	0·318
197·0	0·824	311	0·632	0·477
229·6	1·17	397	0·790	0·651
264·7	1·46	468	0·933	0·800
297·8	1·71	530	1·06	0·953
320·0	1·83	559	1·13	1·00
341·0	1·89	574	1·19	1·06
349·2	1·91	579	1·21	1·08
355·0	1·93	584	1·23	1·09
360·0	1·94	587	1·24	1·10

* Diamagnetic correction, $10^6\Delta = -108$.

Copper formate–β-picoline

Temp. (°K)	$10^6\chi_g$	$10^6\chi_M$ *	μ (B.M.) ($N\alpha = 60 \times 10^{-6}$)	μ (B.M.) ($N\alpha = 168 \times 10^{-6}$)
109·6	0·274	177	0·322	0
121·1	0·219	163	0·317	0
130·5	0·199	158	0·321	0
136·0	0·211	161	0·333	0
145·0	0·219	163	0·347	0
155·9	0·287	180	0·389	0·123
165·8	0·323	189	0·415	0·168
200·7	0·790	304	0·629	0·469
232·5	1·15	393	0·790	0·665
257·5	1·44	464	0·916	0·784
294·7	1·82	558	1·09	0·963
298·6	1·83	560	1·10	0·971
330·4	1·98	597	1·20	1·07
340·0	2·04	612	1·23	1·10
350·0	2·04	612	1·25	1·12
359·5	2·07	620	1·28	1·15
368·9	2·08	622	1·29	1·16

* Diamagnetic correction, $10^6\Delta = -108$.

Copper formate–γ-picoline *

85·0	0·281	177	0·272	0
120·6	0·263	173	0·324	0
130·0	0·282	178	0·337	0
151·3	0·267	174	0·363	0
193·0	0·697	280	0·585	0·418
221·1	1·17	397	0·776	0·639
244·8	1·45	466	0·895	0·767
259·9	1·52	483	0·942	0·813
295·5	1·70	527	1·05	0·925
319·8	1·82	557	1·13	1·00
345·2	1·85	564	1·18	1·05
355·1	1·92	582	1·22	1·09
364·9	1·89	574	1·23	1·09

* Diamagnetic correction, $10^6\Delta = -108$.

Copper formate–hemidioxan †

86·8	0·293	132	0·224	0
90·8	0·280	129	0·225	0
95·0	0·271	128	0·228	0
101·5	0·271	128	0·236	0
109·4	0·275	128	0·245	0
120·9	0·272	128	0·258	0
132·1	0·318	137	0·286	0·098
149·0	0·405	154	0·336	0·177
174·3	0·668	206	0·453	0·331
218·8	1·25	315	0·671	0·574
261·0	1·68	406	0·854	0·765
285·3	1·88	446	0·943	0·855
310·0	2·06	481	1·03	0·939
334·0	2·22	513	1·11	1·02
368·0	2·42	552	1·21	1·11

† Diamagnetic correction, $10^6\Delta = -74$.

Copper acetate–dioxan

Temp. (°K)	$10^6\chi_g$	$10^6\chi_M$ *	$\mu = 2{\cdot}839\,[(\chi_M - 60)T]^{\frac{1}{2}}$
88·0	−0·0838	100	0·169
95·2	−0·0126	120	0·215
103·0	0·161	166	0·297
121·0	0·483	253	0·434
151·4	1·11	422	0·665
173·6	1·50	528	0·809
198·6	1·84	619	0·946
224·6	2·13	698	1·08
258·0	2·34	754	1·20
295·0	2·41	773	1·30

* Diamagnetic correction, $10^6\Delta = -123$.

exposure to moist air (Found: C, 35·2; H, 5·1; Cu, 23·2. $C_8H_{14}O_6Cu$ requires C, 35·6; H, 5·2; Cu, 23·6%).

Magnetic Measurements.—The techniques and corrections applied in this work are essentially those described earlier. Previously, an allowance of $N\alpha = 60 \times 10^{-6}$ was made for the temperature-independent contribution to the paramagnetism per g.-ion of copper. This value was first calculated theoretically by Polder [6] for hexaquocupric ions, and later by Bleaney and Bowers [2] for copper(II) acetate monohydrate on the assumption that the ligand-field splittings are those present in Tutton's salts. The unusual absorption spectra [3,7] of binuclear copper(II) alkanoates provide strong evidence that this assumption is probably unjustified, and that the ligand-field splittings must be considerably modified in these compounds. Fortunately, it has been possible to measure $N\alpha$ directly with some of the compounds here described, the values being 2—3 times greater than those previously calculated. Accordingly, the effective magnetic moments quoted below have been calculated for two values of $N\alpha$; first, by assuming $N\alpha = 60 \times 10^{-6}$ for comparison with earlier data on compounds for which $N\alpha$ is not easily measured, and secondly, with the present experimental values. The experimental data for the compounds now described are tabulated.

Discussion

This work has yielded several new derivatives of copper(II) formate, which at room temperature possess the magnetic properties shown in Table 2 (copper sulphate and copper acetate are included for comparison). The magnetic moments of the mono- and the hemi-dioxan compound of copper acetate fall in the range $\mu = 1{\cdot}34 \pm 0{\cdot}04$ B.M., which are closely similar to the values, $\mu = 1{\cdot}36$ B.M., determined for copper acetate dissolved in dioxan,[3,8] and $\mu = 1{\cdot}39$ B.M. for copper acetate itself.[5]

Table 2. *Room-temperature magnetic data.*

Compound *	Colour	Temp.	Magnetic properties $10^6\chi_g$	$-10^6\Delta$	$10^6\chi_M$	$\mu = 2{\cdot}839\,[(\chi_M - N\alpha)T]^{\frac{1}{2}}$ $N\alpha = 60 \times 10^{-6}$	$N\alpha$ (expt.)
$CuSO_4,5H_2O$	Blue	20·0°	5·90	122	1595	1·91	—
$Cu(CH_3{\cdot}CO_2)_2,H_2O$...	Blue-green	21·0	4·03	85	889	1·40	—
$Cu(H{\cdot}CO_2)_2(an)_2$ ...	Gold lustre	22·7	3·87	172	1489	1·85	—
$Cu(H{\cdot}CO_2)_2$,py	Emerald-green	30·6	1·83	96	523	1·07	0·932
$Cu(H{\cdot}CO_2)_2$,α-pic ...	,,	23·6	1·71	108	530	1·06	0·932
$Cu(H{\cdot}CO_2)_2$,β-pic ...	,,	25·6	1·83	109	560	1·10	0·971
$Cu(H{\cdot}CO_2)_2$,γ-pic ...	,,	22·5	1·70	108	527	1·06	0·925
$Cu(H{\cdot}CO_2)_2,\frac{1}{2}$(diox)	Blue-green	17·0	1·92	74	453	0·96	0·872
$Cu(CH_3{\cdot}CO_2)_2,\frac{1}{2}$(diox)	Green	18·5	3·41	97	866	1·38	—
$Cu(CH_3{\cdot}CO_2)_2$,diox...	Blue-green	20·0	2·40	123	770	1·30	—

an = aniline, py = pyridine, pic = picoline, diox = dioxan.

These derivatives of copper formate fall naturally into two well-defined groups on the basis of their magnetic properties at room temperature. Members of the first group have magnetic moments in the range $\mu = 1{\cdot}9 \pm 0{\cdot}2$ B.M., the value normally observed for magnetically dilute compounds of bivalent copper. These are the well-known royal-blue or violet bisaminecupric compounds $Cu(H{\cdot}CO_2)_2(amine)_2$, and the golden bisaniline derivative.

The remaining derivatives comprise the second group, which is characterized by sub-normal magnetic moments at room temperature (see Table 2). These are the four heterocyclic monoamine derivatives with moments in the range $\mu = 1{\cdot}08 \pm 0{\cdot}02$ B.M., and the hemidioxan compound with $\mu = 0{\cdot}96$ B.M., a value which may be compared with the magnetic moment of copper formate in dioxan solution, $\mu = 1{\cdot}01$ B.M.,[3] where solvation is probably increased to give $[Cu_2(H{\cdot}CO_2)_4(C_4H_8O_2)_2]$ molecules. These moments are even lower than those observed [4] for the heavier binuclear copper n-alkanoates, $\mu = 1{\cdot}38 \pm 0{\cdot}03$ B.M., and likewise are strongly dependent on temperature.

[5] Figgis and Martin, *J.*, 1956, 3837.
[6] Polder, *Physica*, 1942, **9**, 709.
[7] Tsuchida, Yamada, *et al.*, *Nature*, 1955, **176**, 1171; 1956, **178**, 1192; *Bull. Chem. Soc. (Japan)*, 1957, **30**, 953; 1958, **31**, 303.
[8] Kondo and Kubo, *J. Phys. Chem.*, 1958, **62**, 468.

The anomalous temperature variation of the magnetic susceptibility exhibited by each of the compounds in the second group enables their molecular configuration to be readily deduced. Below about 120° K, only a small residual paramagnetism is observed, which is independent of temperature within experimental error, and the compounds have zero magnetic moment (cf. Figs. 1 and 2). At temperatures above *ca.* 120° K, the paramagnetic

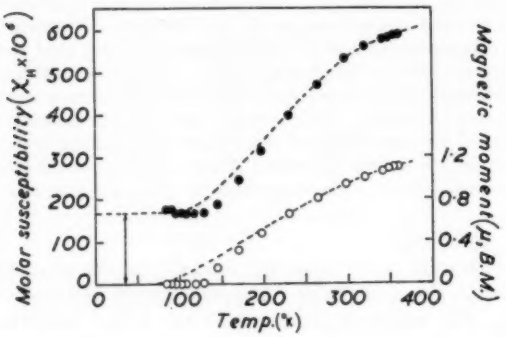


FIG. 1. $[Cu_2(H{\cdot}CO_2)_4(\alpha\text{-}Me{\cdot}C_5H_4N)_2]$.
● χ_M ○ μ ---- Calculated.
The arrow represents $N\alpha = 168 \times 10^{-6}$ (exptl.).

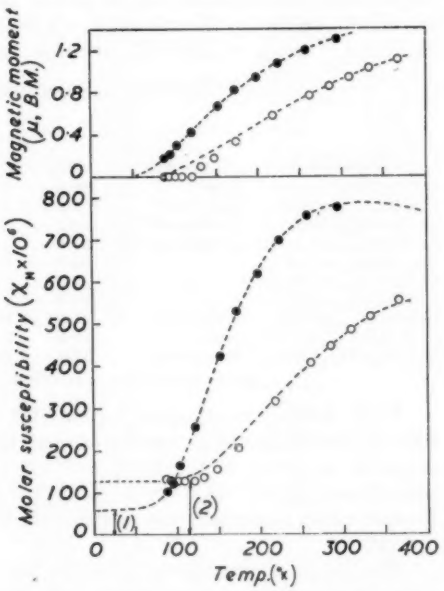


FIG. 2.
● $[Cu_2(Me{\cdot}CO_2)_4(C_4H_8O_2)_2]$.
○ $[Cu_2(H{\cdot}CO_2)_4(C_4H_8O_2)]$.
---- Calculated.
The arrows represent $N\alpha$ = (1) 60×10^{-6} (calc.) and (2) 128×10^{-6} (exptl.).

susceptibility steadily increases until the compounds decompose at 360—370° K. At the decomposition temperature the moments have risen to *ca.* 1·2 B.M.

It is noteworthy that the only other diamagnetic complex of bivalent copper is the dark green binuclear bisdiazoaminobenzene derivative, $Cu_2(Ph{\cdot}N{:}N{\cdot}NPh)_4$, recently reported by Harris and Martin.[9] This is believed to possess the structure (II), the diamagnetism arising from the presence of a strong copper-to-copper bond. Unlike the present compounds, bisdiazoaminobenzenecopper(II) is diamagnetic at all temperatures between 80° and 400° K. We believe that the anomalous magnetic properties of the monoamino- and hemidioxan derivatives of copper formate likewise reflect the presence of

[9] Harris and Martin, *Proc. Chem. Soc.*, 1958, 259.

a direct copper-to-copper exchange interaction arising from the binuclear molecular configuration shown in (I), where L = amine or dioxan.

The binuclear structure proposed for these derivatives of copper formate is supported by a comparison of the experimental susceptibility with that calculated on the basis of the copper acetate type model discussed [5] in Part I. There it was shown that the magnetic susceptibility, χ_M, could be related to the energy interval, J, between a lower singlet state ($S = 0$) and an upper triplet state ($S = 1$) (which arise from direct exchange between pairs of contiguous copper atoms in the molecule) by means of an expression, first derived by Bleaney and Bowers,[2] for copper(II) acetate monohydrate, *viz.*,

$$\chi_M = \frac{g^2N\beta^2}{3kT}\left[1 + \tfrac{1}{3}\exp\left(J/kT\right)\right]^{-1} + N\alpha$$

where J was evaluated from the relation, $J = 1{\cdot}6kT_c$, T_c representing the temperature at which the susceptibility attains its maximum value. Unfortunately, T_c cannot be measured for the present derivatives, since they decompose well below this temperature, and so g, the spectroscopic splitting factor, of necessity, has been taken to be the mean of the values obtained for the higher homologues, *i.e.*, $g = 2{\cdot}16$, and T_c obtained from it for each compound by substituting into the equation the value of χ_M at three temperatures, 150°, 250°, and 350° K. Thereby, it is found that J is not independent of temperature, as is assumed in the derivation of the above formula, but that it differs considerably at 150° from the values at 250° and 350°. The values at the two higher temperatures are, however, in close agreement and in the calculation of the theoretical susceptibility curves for the four amine derivatives, T_c and J are accordingly taken as the mean of the values obtained for the four compounds at 250° and 350° K. Table 3 contains the calculated values of T_c for the four amines and the dioxan compound at the three temperatures: the values at 150° will naturally show large scatter owing to the small magnitude of the susceptibility at such low temperatures.

The calculated susceptibility equations for the five compounds then become

$$[Cu_2(H{\cdot}CO_2)_4(\text{amine})_2] \ldots\ldots \chi_M = \frac{0{\cdot}585}{T}\left[1 + \tfrac{1}{3}\exp.\left(\frac{776}{T}\right)\right]^{-1} + 168 \times 10^{-6}$$

$$[Cu_2(H{\cdot}CO_2)_4(C_4H_8O_2)] \ldots\ldots \chi_M = \frac{0{\cdot}585}{T}\left[1 + \tfrac{1}{3}\exp.\left(\frac{794}{T}\right)\right]^{-1} + 128 \times 10^{-6}$$

TABLE 3. *Calculated values of* T_c *at* 150°, 250°, *and* 350° K.

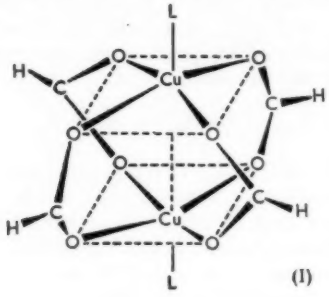
Derivative	T_c (calc.) 150°	250°	350°
Pyridine	569	489	495
α-Picoline	553	484	484
β-Picoline	—	484	461
γ-Picoline	628	480	491
Dioxan	565	502	497

The data for the α-picoline derivative are representative of the behaviour of the amine complexes, and are plotted in Fig. 1. The agreement between the calculated and experimental curves is quite good if allowance is made for the appreciable increase in magnitude of J as the temperature is lowered below 250° K. This agreement provides strong evidence that the compounds are indeed binuclear derivatives of copper formate with the structure (I), and should be properly formulated as $[Cu_2(H{\cdot}CO_2)_4am_2]$ and $[Cu_2(H{\cdot}CO_2)_4(C_4H_8O_2)]$.

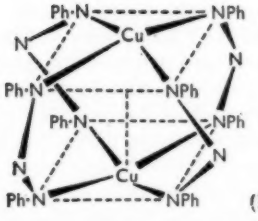
Table 4 contains values, calculated from the expression $J = 1{\cdot}6kT_c$, for the separation between the singlet and triplet states. It will be seen that for these compounds J is of the order of 500—600 cm.$^{-1}$ (*i.e.*, 1·5—2·0 kcal. mole^{-1}), which is roughly twice the separation observed [4] in the heavier anhydrous and hydrated copper n-alkanoates, where $J = 309 \pm 31$ cm.$^{-1}$ $= 0{\cdot}88 \pm 0{\cdot}09$ kcal mole^{-1}. This is an indication that the intramolecular exchange interaction between copper atoms is considerably stronger in the formate series.

That this stronger interaction arises from the replacement of acetate by formate,

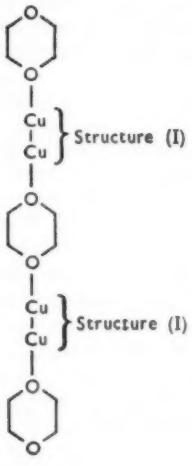
and not by the insertion of amine or dioxan in the terminal positions, is demonstrated by direct comparison of the dioxan derivatives of copper formate and copper acetate. The susceptibility–temperature and magnetic moment–temperature curves for both $[Cu_2(H{\cdot}CO_2)_4(C_4H_8O_2)]$ and $[Cu_2(CH_3{\cdot}CO_2)_4(C_4H_8O_2)_2]$ are plotted together in Fig. 2. The magnetic moment of the acetate derivative rises from zero to 1·5 B.M. in



(I)



(II)



(III)

the temperature range 50—400° K, in contrast to the moment of the formate derivative which is zero below 120° K, and has only increased to 1·2 B.M. at 400° K. Similarly, while the χ–T curve for acetate exhibits a well-defined maximum at 325° K, there is no evidence

TABLE 4. *Calculated separation between singlet and triplet levels at* 150°, 250°, *and* 350° K, g *being assumed to be* 2·16.

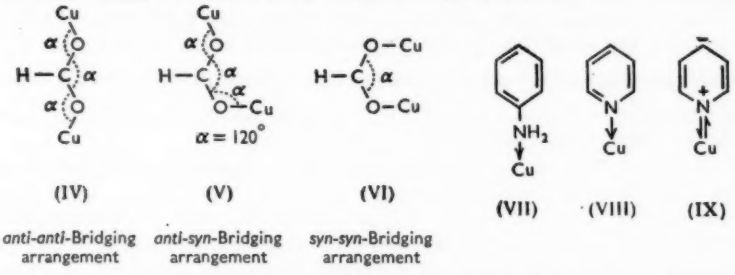
Compound $[Cu_2(H{\cdot}CO_2)_4L_2]$	150°		250°		350°	
Singlet-triplet separation, J	cm.$^{-1}$	kcal. mole^{-1}	cm.$^{-1}$	kcal. mole^{-1}	cm.$^{-1}$	kcal. mole^{-1}
L = Pyridine	632	1·81	543	1·55	550	1·57
α-Picoline	614	1·75	538	1·54	538	1·54
β-Picoline	—	—	538	1·54	512	1·46
γ-Picoline	701	2·00	534	1·53	546	1·56
Mean for amine derivatives	649 ± 52	1·85 ± 0·15	538 ± 5	1·54 ± 0·01	537 ± 25	1·53 ± 0·07
L_2 = Dioxan	628	1·80	558	1·60	552	1·58

for a maximum in the formate curve up to 375° K, and, in fact, the calculated value is as high as 497° K. Evidently, replacement of acetate by the formate ion markedly increases the proposed $3d_{z^2}$–$3d_{z^2}$ orbital overlap, and thereby enhances the depression of the magnetic moment.

The shape of the susceptibility–temperature curves for the binuclear formate derivatives differs from that of the heavier alkanoates in one further significant feature, namely, the constant value recorded for the susceptibility below about 120° K. This value for the four amine complexes falls in the range $(168 \pm 10) \times 10^{-6}$, whilst for the hemidioxan compound a slightly smaller value, 128×10^{-6}, was recorded. The constant susceptibilities at low temperatures represent the temperature-independent paramagnetism associated with bivalent copper and will be discussed elsewhere.[10] The fact that this paramagnetism

[10] Lark, Martin, and Waterman, unpublished data.

is being observed in the complete absence of spin paramagnetism shows that, at these temperatures, all the copper atoms are in diamagnetic singlet states, and that only above 120° K do the paramagnetic triplet states begin to be populated.



It is interesting that the dichroic dark blue-green dioxan derivative contains only one dioxan molecule per binuclear formate molecule. This immediately suggests that dioxan is utilizing both its oxygen atoms by co-ordinating with copper atoms from two different binuclear molecules. It would thus act as a novel type of " bridge " enabling the formate molecules to form infinite dioxan-bridged chains. The compound is surprisingly stable to heat, remaining unchanged *in vacuo* even at 150° C. This is in marked contrast to the thermo-sensitive heterocyclic amine derivatives and is quite possibly a consequence of the proposed polymeric structure illustrated in (III).

It is clear from these and earlier investigations that the terminal ligands, marked L in (I), exert such a highly specific influence on the bound copper atom that they largely determine whether the formate will adopt a binuclear configuration or not. It has already been pointed out [1] that the residual electrostatic charge on each copper atom, after bonding, must play an important rôle in deciding whether the bridged dimeric structure will be adopted preferentially. Thus a large residual charge, of either sign, will favour the *anti-anti-* or *anti-syn*-bridging arrangements (IV) and (V), in which bridged copper atoms are *ca.* 5·8 Å apart, rather than the *syn-syn*-arrangement (VI) in which these atoms are virtually contiguous, *i.e.*, *ca.* 2·6 Å apart. The higher acid dissociation constant of formic acid ($K_A = 1{\cdot}7 \times 10^{-4}$) than of, *e.g.*, acetic acid ($K_A = 1{\cdot}7 \times 10^{-5}$) reflects the smaller σ-electron charge density on the formate oxygen atoms. It seems not unreasonable to infer that the formate will therefore be less effective than acetate in reducing the positive charge on copper during the formation of the relevant copper n-alkanoate. This could well account for the reluctance of copper formate to crystallize from dilute formic acid solution with the binuclear configuration based on the *syn-syn*-configuration (VI). Nevertheless, the visible and ultraviolet spectra of such solutions do provide evidence for the ephemeral existence of such a species, even though it could not be isolated from solution either in hydrated or anhydrous forms.[1]

The remarkable " conditioning " influence exerted on copper formate by the pyridine bases and by dioxan, when occupying the terminal positions L in (I), can thus arise from the concomitant reduction in magnitude of the residual positive charge on each copper atom, to an extent sufficient for the *syn-syn*-bonding arrangement to become the favoured configuration. The fact that conversion of the violet bisamine cupric formates into the emerald-green monoamine derivates takes place so readily in the solid state, even under mild conditions, indicates that the binuclear configuration is much the preferred structure, provided that the magnitude of the electrostatic charge in copper has been reduced below some critical value. Since α-picoline is as efficient as pyridine in effecting this change, it is concluded that any inductive or steric effects due to the α-methyl group are either absent or very small.

The success of the pyridine-type bases contrasts with the failure of aniline in inducing the bridged configuration. However, pyridine co-ordinates to transition-metal ions, both

more frequently and more strongly than aromatic amines, for whereas aniline can only form a classical co-ordinate link as in (VII), pyridine can form a multiple bond to the metal atom which involves both an $\overset{+}{N}\rightarrow\overline{M}$ classical co-ordinate σ-linkage and a $\overset{+}{M}\rightarrow\overline{N}$ ($3d_\pi\rightarrow 2p_\pi$) bond, through participation of the structures (VIII) and (IX). Double bonding between the metal and pyridine immediately provides a mechanism by which an excessive accumulation of negative charge on copper from the $\overset{+}{N}\rightarrow\overline{Cu}$ σ-bond can be partly alleviated by means of the $\overset{+}{Cu}\rightarrow\overline{N}$, π-bond, which has the reverse polarity. In the case of aniline no such mechanism exists.

In addition to double-bonding capacity, the subtle influence of the terminal ligand L must result from the accumulated influence of a variety of other factors. Both the electrostatic and orbital (*e.g.*, $3d_z^2$–$3d_z^2$) Cu–Cu repulsions, and the electronegativity, polarizability, σ-electron charge density, steric environment, and compatibility of L–Cu orbital overlap, of the ligating atom, are all factors which must contribute to its influence when co-ordinated to copper in this way. Obviously, it is impossible to disentangle the individual contributions of each effect from a magnetic moment which is indirectly related to the total accumulated contribution. The range of the positive and negative residual charges in which the *syn-syn*-arrangement is stable is probably narrow.

Finally, it is noteworthy that pyridine and its three methyl derivatives, and the cyclic aliphatic diether, dioxan, not only force copper formate to adopt the δ-bonded structure, but lead to the formation of a copper-to-coper δ-bond of greater binding energy than the δ-bond in heavier copper n-alkanoates. This is indicated by the much lower magnetic moment of the formate derivatives at room temperature (0·9 B.M. compared with 1·4 B.M.), and by the higher temperature of the maximum susceptibility (about 500° K compared with 270° K). In fact, the singlet–triplet separation, J, which provides a measure of the exchange energy associated with the δ-bond, is nearly twice that observed in copper n-alkanoates, reflecting a greatly enhanced lateral overlap between the Cu–Cu, $3d_{\delta}$–$3d_{\delta}$, orbitals.

The increased δ-overlap may arise as follows. First, it is possible that the Cu–Cu distance in the formate derivatives is decreased from the value of 2·64 Å observed in copper acetate monohydrate, towards the value 2·55 Å observed in metallic copper. It has already been pointed out [5] that orbital overlap between two δ-orbitals oriented with their lobar planes parallel will be particularly sensitive to the separation between their centres. Dr. G. A. Barclay and C. Kennard, of this department, are engaged on an *X*-ray structural investigation of the monopyridine derivative, in order to determine both the molecular geometry and the Cu–Cu bond length.

The second possibility assumes that the Cu–Cu distance remains 2·64 Å, as in the acetate, but that the $3d_{\delta}$–$3d_{\delta}$ overlap is considerably enhanced by the modified ligand field produced by the replacement of acetate by formate oxygen atoms and the presence of the terminal ligands. Thus, we [11] have recently prepared binuclear compounds of the type $[Cu_2(C_3H_7{\cdot}CO_2)_4py_2]$ with a moment of 1·37 (20°) and $J = 300$ cm.$^{-1}$, which contrast with the corresponding aniline analogue $[Cu_2(C_3H_7{\cdot}CO_2)_4an_2]$ which has a much higher moment 1·8 B.M. and lower $J = 100$ cm.$^{-1}$. Clearly, in this series, the terminal ligand is exerting a marked influence on the $3d_{\delta}$–$3d_{\delta}$ orbital overlap. The preparation of new binuclear derivatives of bivalent copper of general formula $[Cu_2(R{\cdot}CO_2)_4L_2]$, and the effect of varying both R and L on the magnetic properties and on the binding energy of the Cu–Cu δ-bond, will be reported in a forthcoming publication.

The authors thank Dr. E. Challen for carbon, hydrogen, and nitrogen microanalyses. One of them (H. W.) is indebted to the Australian Atomic Energy Commission for a Studentship during the tenure of which this work was carried out.

School of Chemistry, University of New South Wales,
Sydney, Australia. [*Received, October* 13*th*, 1958.]

[11] Kokot and Martin, unpublished data.

XUM

594. *The Conversion of Carbamoylmethyl Thiolsulphates into Thio-oxamides; a New Variant of the Willgerodt–Kindler Reaction.*

By Brian Milligan and J. M. Swan.

Substituted thio-oxamides (II) are obtained in 21—96% yield by heating carbamoylmethyl thiolsulphates (I) with a primary or secondary amine. A mechanism proposed for the reaction invokes formation of a thioaldehyde and then of either an anil or a substituted diaminomethane from which the product is derived by a Willgerodt–Kindler reaction.

Nomenclature.—Symmetrical and unsymmetrical disubstituted monothio-oxamides (II) are described here for the first time. The Editor has suggested that we name them as derivatives of thio-oxamide using prefixes N^O- and N^S- to indicate the nitrogen atoms next to CO and CS respectively (cf. the use of N^1 and N^4 for sulpha drugs). Hence (IIa) (R = Ph, R′ = C_6H_{11}) is N^S-cyclohexyl-N^O-phenyl(thio-oxamide), the parentheses being necessary since " phenylthio " would denote PhS. When one of the nitrogen atoms is involved in ring formation this method is abandoned and a rule made that Ph·NH·CO·CS– is named *N*-phenyl-α-thio-oxamoyl. Thus the product obtained by heating sodium phenylcarbamoylmethyl thiolsulphate (I; R = Ph) with morpholine, namely, (IIb; R = Ph, R_2'' = –CH_2·CH_2·O·CH_2·CH_2–), is named 4-(phenyl-α-thio-oxamoyl)-morpholine.

In a study of azo-dyes and other compounds containing thiolsulphate groups, we have found that various carbamoylmethyl thiolsulphates (I) react with primary or secondary amines when heated, to give substituted thio-oxamides (II):

$$\underset{\text{(I)}}{\text{R·NH·CO·CH}_2\text{·S·SO}_3\text{Na}} \xrightarrow{\text{R'NH}_2 \text{ or } \text{R}_2''\text{NH}} \underset{\text{(IIa)}}{\text{R·NH·CO·CS·NHR'}} \text{ or } \underset{\text{(IIb)}}{\text{R·NH·CO·CS·NR}_2''}$$

In compounds (I) the group R was hydrogen, phenyl, cyclohexyl, 4-phenylazophenyl, or 1-phenylazo-2-naphthyl, and the amines used were cyclohexylamine, aniline, morpholine, and allylamine. The reaction was carried out most readily by boiling the sodium alkyl thiolsulphate (Bunte salt) with an excess of the anhydrous amine; reaction times varied between three and thirty minutes. N^S-Cyclohexyl-N^O-phenyl(thio-oxamide) (IIa; R = Ph, R′ = C_6H_{11}) was also obtained by fusion of cyclohexylammonium phenylcarbamoylmethyl thiolsulphate. It is noteworthy that with cyclohexylamine good yields of thio-oxamides were obtained in some cases when the reaction was carried out in aqueous solution at 100°. For example, the amides (IIa; R = Ph·N_2·C_6H_4 and Ph·N_2·$C_{10}H_6$, R′ = C_6H_{11}) were obtained in this manner from the salts (I) in 86% and 96% yield respectively. The salt (I; R = Ph·N_2·C_6H_4) failed to react with liquid ammonia, and with boiling aqueous ammonia gave di-(*p*-phenylazophenylcarbamoylmethyl) disulphide. Reaction of the analogous salt (I; R = Ph·N_2·$C_{10}H_6$) with boiling aqueous ammonia also gave a disulphide; and sodium cyclohexylcarbamoylmethyl thiolsulphate (I; R = C_6H_{11}) gave the corresponding disulphide and a small amount of *N*-cyclohexyloxamide. The last product is probably derived from an intermediate thio-oxamide by desulphurisation in the ammoniacal solution.[1]

Although sodium phenylcarbamoylmethyl thiolsulphate (I; R = Ph), when heated to boiling in aqueous cyclohexylamine, gave the thio-oxamide (IIa; R = Ph, R′ = C_6H_{11}) in 55% yield, it failed to react in aqueous aniline, and in aqueous morpholine gave a high yield of di(phenylcarbamoylmethyl) disulphide. Heating sodium benzyl thiolsulphate in aqueous or anhydrous amines gave dibenzyl disulphide, no trace of any thiobenzamide being isolated. The reaction also failed when a second methylene group was introduced between the carbamoyl and the thiolsulphate radical. Thus, after sodium 2-(phenylcarbamoyl)-

[1] Bernthsen, *Annalen*, 1877, **184**, 290.

ethyl thiolsulphate had been heated in cyclohexylamine or morpholine at 135° for 10 min., unchanged Bunte salt (70%) and di-(2-phenylcarbamoylethyl) disulphide (20%) were isolated.

By heating thiolsulphates with amines we hoped initially to synthesise sulphenamides according to the equation $R{\cdot}S{\cdot}SO_3Na + R'{\cdot}NH_2 \longrightarrow RS{\cdot}NHR' + NaHSO_3$. Such sulphenamides derived from (I) would be hardly distinguishable by analysis (two hydrogen atoms) from the thio-oxamide (II). However, oxidation of the new compounds with peracetic acid caused desulphurisation with formation of oxamides, whereas sulphenamides would have been converted into sulphonamides without loss of sulphur. The oxamides were identified by analysis and in some cases by comparison of melting points with recorded values. It was also necessary to establish that the thioamide group was derived from the $\cdot CH_2{\cdot}S{\cdot}SO_3^-$ unit, and not from the carbamoyl group, with simultaneous conversion of $\cdot CH_2{\cdot}S{\cdot}SO_3^-$ into $\cdot CO{\cdot}NRR'$. Heating sodium carbamoylmethyl thiolsulphate (I; R = H) with aniline gave the expected N^S-phenyl(thio-oxamide) (IIa; R = H, R′ = Ph) and not the isomeric N^O-phenyl (thiooxamide) (IIa; R = Ph, R′ = H). Identity was established by m. p. and by oxidation with ferricyanide to benzothiazole-2-carboxyamide.[2]

The formation of thio-oxamides by reaction of Bunte salts with amines has an obvious similarity to the Kindler reaction [3-5] which, developed as a variant of the Willgerodt reaction,[4,5] consists in the conversion of aromatic aldehydes and aryl ketones into aryl alkyl thioamides or ω-aryl-aliphatic thioamides by anhydrous amines and sulphur at high temperatures. The appropriate aldimine or ketimine (Schiff's bases) can be used in place of the mixture of carbonyl compound and amine,[3,6] and derivatives of acids are also formed by heating ketoximes, azines, hydrazones, etc., with sulphur.[7] Furthermore, the phenylmethylenediamine derived from benzaldehyde and morpholine yields benzothiomorpholide when heated with sulphur; [8] benzylamine and sulphur give *N*-benzylthiobenzamide; [9] diethylamine and sulphur give *N*-ethylthioacetamide; [10] and dibenzyl disulphide with morpholine and sulphur yields benzothiomorpholide.[8] We have shown that heating sodium benzyl thiolsulphate with morpholine and sulphur also gives benzothiomorpholide, whereas in the absence of added sulphur only dibenzyl disulphide is obtained. In our reaction of carbamoylmethyl thiolsulphate with amines, the sulphur required by the Kindler reaction must be made available from the thiolsulphate radical by some process peculiar to this class of Bunte salt.

The following mechanism is proposed. As the first step we envisage nucleophilic elimination of sulphite ion from the " inner " sulphur atom of the $\cdot S{\cdot}SO_3^-$ group, as in nucleophilic elimination of groups such as halogen, $\cdot NR_3^+$ and $\cdot SR_2^+$ from carbon. Thus if B: is a base, we write:

$$B: + -\overset{\beta}{C}H_2-\overset{\alpha}{S}-SO_3^- \longrightarrow BH^+ + -CH{=}S + SO_3^{2-}$$

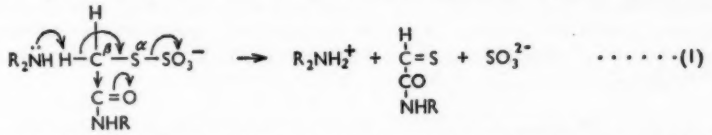
$$\text{Cf.}\quad B: + -\overset{\beta}{C}H_2-\overset{\alpha}{C}H_2-X \longrightarrow BH^+ + -CH{=}CH_2 + X^-$$

As with the olefin-forming *E*2 reaction,[11] this elimination of sulphite should be facilitated by electron-attracting groups on the β-carbon atom. This may explain the apparent necessity for the carbamoyl group at this position, so that the synchronous

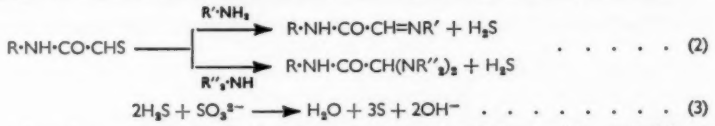
[2] Reissert, *Ber.*, 1904, **37**, 3708.
[3] Kindler, *Annalen*, 1923, **431**, 187; *Arch. Pharm.*, 1927, **265**, 389.
[4] Carmack and Spielman, *Organic Reactions*, 1946, **3**, 83.
[5] McOmie, *Ann. Reports*, 1948, **45**, 210.
[6] Böttcher and Bauer, *Annalen*, 1950, **568**, 218.
[7] Stanck, *Coll. Czech. Chem. Comm.*, 1947, **12**, 671.
[8] King and McMillan, *J. Amer. Chem. Soc.*, 1948, **70**, 4143.
[9] McMillan, *ibid.*, p. 868.
[10] Moore and Saville, *J.*, 1954, 2083.
[11] Ingold, " Structure and Mechanism in Organic Chemistry," Bell & Sons Ltd., London, 1953, Chap. VIII.

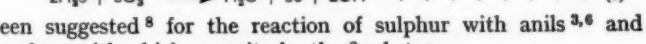
displacement can be pictured as in step 1. The thioaldehyde formed then reacts with further amine to give hydrogen sulphide and either an anil or a substituted diaminomethane (step 2); the hydrogen sulphide liberated reacts with sulphite to form sulphur (step 3).

Step 3 is justified by the observation that a solution of sulphur dioxide or sodium

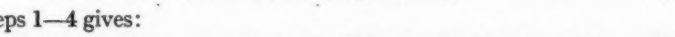


hydrogen sulphite in boiling cyclohexylamine reacted with hydrogen sulphide to give a dark mixture containing free sulphur. When this mixture was poured into water, large amounts of thiosulphate derived from sulphur and unchanged sulphite were detected.

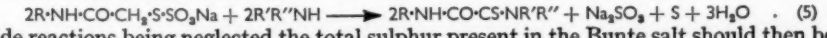




A mechanism has been suggested [8] for the reaction of sulphur with anils [3,6] and methylenediamines,[8] by analogy with which we write for the final step:



Summation of steps 1—4 gives:



Side reactions being neglected the total sulphur present in the Bunte salt should then be accounted for as thioamide (50%), sulphite (25%), and sulphur (25%), or as smaller amounts of sulphite and sulphur with corresponding amounts of thiosulphate. In fact, when sodium phenylcarbamoylmethyl thiolsulphate was supended in cyclohexylamine, heated under reflux for 5 minutes, and then poured into water, the total sulphur was accounted for as thio-oxamide (42·3%), sulphide (1·3%), sulphite (17·6%), and thiosulphate (31·6%).

It follows from the above mechanism that the sulphur in the thio-oxamide arises from *both* of the sulphur atoms initially present in the Bunte salt. A sample of sodium phenylcarbamoylmethyl thiolsulphate labelled with ^{35}S in the SO_3^- group was prepared by the exchange which occurs between a Bunte salt and sulphite ion in aqueous solution: [12]

When labelled material was heated in cyclohexylamine, radioactivity was found both in the inorganic salts and in the thio-oxamide. While not proving our mechanism, this appears to exclude * any process involving a continuous attachment of the " inner " sulphur atom of the thiolsulphate group to the methylene carbon atom, at least for the reaction carried out in anhydrous medium.

If step 1 is indeed the first step of the reaction it constitutes a novel kind of elimination, not only because the electron shells which remain complete throughout the co-operative displacement are shared by a carbon–sulphur bond rather than a carbon–carbon pair, but

* *Added, June 30th*, 1959.—It is possible that the radioactive label could be introduced into the thio-oxamide by an exchange process, so that postulation of carbon–sulphur fission (step 1) would no longer be necessary. However, when a mixture of N^S-cyclohexyl-N^O-phenyl[^{35}S](thio-oxamide) and sodium carbamoylmethyl thiolsulphate was heated in cyclohexylamine the original thio-oxamide was found to have retained all its activity, whereas the newly synthesised N^S-cyclohexyl(thio-oxamide) was non-radioactive. Similarly, when sodium phenylcarbamoylmethyl thiolsulphate was heated in cyclohexylamine containing potassium[^{35}S]sulphide and sulphur, the thio-oxamide formed was radioactive, whereas when this same (unlabelled) thio-oxamide was heated in the cyclohexylamine–sulphur mixture, virtually no exchange occurred.

[12] Fava and Pajaro, *J. Amer. Chem. Soc.*, 1956, **78**, 5203; Swan, *Nature*, 1957, **180**, 643; Fava and Iliceto, *J. Amer. Chem. Soc.*, 1958, **80**, 3478.

also because the ejected sulphite anion already holds a formal negative charge before reaction. In most examples of the olefin-forming elimination,[11] the group displaced is initially either formally positive or neutral. Nucleophilic displacement from sulphur has also been invoked by Rosenthal and Oster [13] to explain the alkaline decomposition of certain disulphides (step 6), although in other cases, particularly with cystine derivatives, the disulphide breakdown appears to be the consequence of a more conventional olefin-forming elimination [14] with fission of a carbon–sulphur bond and elimination of a disulphide anion, $RS{\cdot}S^-$ (step 7).

$$B: + R{\cdot}\overset{\beta}{C}H_2{-}\overset{\alpha}{S}{-}S{-}CH_2R \longrightarrow BH^+ + R{\cdot}CH{=}S + R{\cdot}CH_2{\cdot}S^- \quad (6)$$

$$B: + R_2\overset{\beta}{C}H{-}\overset{\alpha}{C}H_2{-}S{\cdot}SR' \longrightarrow BH^+ + R_2C{=}CH_2 + R'S{\cdot}S^- \quad (7)$$

Nucleophilic displacement of sulphur (as S_2) from a *nitrogen* atom has been proposed by Saville [15] to explain the formation of dibenzylamine and *N*-benzyl(thiobenzamide) from *NN'*-dithiobisdibenzylamine at 140°. The displacement step is written as:

$$(Ph{\cdot}CH_2)_2N^- \cdots H{-}\underset{Ph}{CH}{-}\underset{CH_2Ph}{N}{-}S{-}S^+ \longrightarrow (Ph{\cdot}CH_2)_2NH + Ph{\cdot}CH{=}N{\cdot}CH_2Ph + S_2$$

and, as in our case, the sulphur liberated is then supposed to combine with the Schiff's base by a Kindler reaction to give *N*-benzyl(thiobenzamide).

An alternative to step 1 might be to assume that the first product is a sulphenamide (see above) which then undergoes the elimination:

$$B: + R{\cdot}NH{\cdot}CO{\cdot}CH_2{\cdot}S{\cdot}NR'R'' \longrightarrow BH^+ + R{\cdot}NH{\cdot}CO{\cdot}CH{=}S + R'R''N^-$$

Since aromatic Bunte salts are not capable of transformation into thioamides, they might possibly yield sulphenamides with amines. When sodium *o*-nitrophenyl thiolsulphate was heated with aniline or cyclohexylamine, di-(*o*-nitrophenyl) disulphide was obtained in high yield, but potassium phenyl thiolsulphate was recovered unchanged from similar experiments.

Alkyl thiolsulphates are known to react readily with aqueous cyanide to give thiocyanates and sulphite ion.[16] However, reaction of sodium phenylcarbamoylmethyl thiolsulphate with aqueous potassium cyanide gave 3-phenylpseudothiohydantoin, isomeric with the linear thiocyanate. This result could be expected on the basis of the known reaction of ω-chloroacetanilide with potassium thiocyanate, since the ω-thiocyanoacetanilide first formed cyclises to 3-phenylpseudothiohydantoin which in turn can isomerise to 2-phenyliminothiazolid-4-one.[17]

3-Phenylpseudothiohydantoin gave N^S-cyclohexyl-N^O-phenyl(thio-oxamide) in 23% yield when heated with cyclohexylamine, but no thio-oxamide was derived from the isomeric 2-phenyliminothiazolid-4-one. Phenylcarbamoylmethyl thiolcarbamate also gave the thio-oxamide in low yield on reaction with cyclohexylamine.

Experimental

Light petroleum refers to the fraction of b. p. 55—70° unless otherwise stated. Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory.

Sodium p-*Thiolsulphatoacetamido*(*azobenzene*).—*p*-Aminoazobenzene was converted into its *chloroacetyl* derivative in 77% yield by Ronwin's method.[18] This crystallised from ethanol as yellow needles, m. p. 153° (Found: C, 61·9; H, 4·6; N, 14·9. $C_{14}H_{12}ON_3Cl$ requires C, 61·5; H, 4·4; N, 15·4%).

A solution of sodium thiosulphate pentahydrate (8·5 g.) in water (170 ml.) was added to a

[13] Rosenthal and Oster, *J. Soc. Cosmetic Chemists*, 1954, **5**, 286.
[14] Tarbell and Harnish, *Chem. Rev.*, 1951, **49**, 1; Swan, *Nature*, 1957, **179**, 965.
[15] Saville, *J.*, 1958, 2880.
[16] Footner and Smiles, *J.*, 1925, **127**, 2887.
[17] Wheeler and Johnson, *Amer. Chem. J.*, 1902, **28**, 121.
[18] Ronwin, *J. Org. Chem.*, 1953, **18**, 127.

boiling solution of *p*-chloroacetamidoazobenzene (9·5 g.) in ethanol (170 ml.) and the mixture heated under reflux for 30 min. The resulting clear solution was allowed to cool, whereupon the Bunte *salt* separated as orange plates (11·5 g., 95%). For analysis it was recrystallised once from water and then twice from ethanol (Found: C, 45·1; H, 3·6; S, 17·3. $C_{14}H_{12}O_4N_3S_2Na$ requires C, 45·0; H, 3·2; S, 17·2%).

Di-(p-*phenylazophenylcarbamoylmethyl*) *Disulphide*.—(i) A solution of the preceding salt (1·5 g.) and sodium mercaptoacetate (2·0 g.) in water (60 ml.) was heated on a steam-bath for 1 hr., then cooled, and the *product* (1·35 g., 97%) was filtered off, washed, dried, and crystallised from aqueous *NN*-dimethylformamide as pale orange needles, m. p. 209° (Found: C, 62·6; H, 4·6; S, 11·6. $C_{28}H_{24}O_2N_6S_2$ requires C, 62·2; H, 4·4; S, 11·8%).

(ii) Concentrated hydrochloric acid (2·5 ml.) was heated with the same salt (2·4 g.) in ethanol (120 ml.) for 45 min. Water was added and the resulting flocculent precipitate (1·0 g.) was filtered off. After several crystallisations from ethanol the disulphide (0·3 g.), m. p. 208°, was obtained. A small amount of *p*-aminoazobenzene was isolated from the mother-liquors.

(iii) Excess of bromine water was added to a solution of the salt (1·0 g.) in water (40 ml.), and part of the flocculent precipitate was separated by centrifugation. Crystallisation from aqueous *NN*-dimethylformamide gave the disulphide, m. p. 208°.

(iv) Addition of 30% aqueous ammonia (5 ml.) to a boiling solution of the salt (0·5 g.) in water (30 ml.) gave the disulphide, m. p. 202° after one crystallisation from 2-methoxyethanol.

N^S-*Cyclohexyl*-N^O-p-*phenylazophenyl*(*thio-oxamide*).—Cyclohexylamine (2 ml.) was added to a hot solution of the Bunte salt (2·0 g.) in water (30 ml.), and the mixture was boiled for 5 min. The precipitated *thioamide* (1·6 g., 82%) crystallised from aqueous *NN*-dimethylformamide as orange leaflets, m. p. 180° (Found: C, 65·8; H, 6·1; N, 15·1; S, 8·7. $C_{20}H_{22}ON_4S$ requires C, 66·3; H, 6·1; N, 15·5; S, 8·8%).

Sodium 1-*Phenylazo*-2-*thiolsulphatoacetamidonaphthalene*.—2-*Chloroacetamido*-1-*phenylazonaphthalene*, obtained in 67% yield from 1-phenylazo-2-naphthylamine, crystallised from ethanol as red needles, m. p. 131° (Found: C, 66·6; H, 4·5; N, 12·5. $C_{18}H_{14}ON_3Cl$ requires C, 66·8; H, 4·3; N, 13·0%).

The chloroacetyl derivative (4·3 g.) was converted into the Bunte *salt* in the usual way. The mixture was evaporated under reduced pressure, and the residue extracted with boiling ethanol. Addition of ether precipitated the salt (3·4 g., 61%) as an orange powder. A sample was prepared for analysis by crystallisation from ethanol–ether (Found: C, 49·0; H, 3·6; S, 14·5. $C_{18}H_{14}O_4N_3S_2Na,H_2O$ requires C, 48·9; H, 3·6; S, 14·5%).

Di-(1-*phenylazo*-2-*naphthylcarbamoylmethyl*) *Disulphide*.—(i) Addition of bromine-water to an aqueous solution of the preceding salt gave an immediate flocculent orange precipitate, which was collected by centrifugation and crystallised from aqueous *NN*-dimethylformamide. The *disulphide* separated as red needles, m. p. 201° (Found: C, 67·9; H, 4·6; S, 9·8. $C_{36}H_{28}O_2N_6S_2$ requires C, 67·5; H, 4·4; S, 10·0%).

(ii) Addition of 15N-ammonia (3 ml.) to a solution of the salt (0·35 g.) in boiling water (15 ml.) gave an orange-red precipitate. One crystallisation from aqueous *NN*-dimethylformamide gave the disulphide (0·1 g.), m. p. 198°.

N^S-*Cyclohexyl*-N^O-1-*phenylazo*-2-*naphthyl*(*thio-oxamide*).—Reaction of the 2-naphthyl Bunte salt with cyclohexylamine as described above gave the *thio-oxamide* in 96% yield. It crystallised from aqueous *NN*-dimethylformamide as red needles, m. p. 184° (Found: C, 69·3; H, 5·8; N 13·0; S, 8·1. $C_{24}H_{24}ON_4S$ requires C, 69·2; H, 5·8; N, 13·5; S, 7·7%).

Sodium Phenylcarbamoylmethyl Thiolsulphate.—This Bunte salt, obtained in 90% yield by reaction of ω-chloroacetanilide with sodium thiosulphate in the usual way, crystallises from water as a monohydrate.[19]

Cyclohexylammonium Phenylcarbamoylmethyl Thiolsulphate.—Cyclohexylamine (0·6 ml.) was added to a solution of the preceding salt (1·0 g.) in hot water (15 ml.) containing acetic acid (0·6 ml.). On cooling, the *cyclohexylammonium salt* (1·1 g.) separated as plates, m. p. 135·5° (Found: N, 7·7; S, 18·6. $C_{14}H_{22}O_4N_2S$ requires N, 8·1; S, 18·5%).

Aniline Phenylcarbamoylmethyl Thiolsulphate.—This *salt*, similarly prepared, crystallised from water as plates, m. p. 180° (Found: S, 18·4. $C_{14}H_{16}O_4N_2S_2$ requires C, 18·5%).

N^S-*Cyclohexyl*-N^O-*phenyl*(*thio-oxamide*).—(i) Cyclohexylamine (0·6 ml.) was added to a solution of sodium phenylcarbamoylmethyl thiolsulphate (1·0 g.) in boiling water (20 ml.). The yellow oil (0·54 g., 55%) which separated gave the *thio-oxamide* as yellow needles, m. p. 130°

[19] Weiss and Sokol, *J. Amer. Chem. Soc.*, 1950, **72**, 1687.

XUM

(from ethanol) (Found: C, 64·4; H, 6·9; N, 10·4; S, 12·1. $C_{14}H_{18}ON_2S$ requires C, 64·1; H, 6·9; N, 10·6; S, 12·1%).

(ii) (*a*) The sodium salt (2·25 g.) was suspended in cyclohexylamine (5 ml.) and heated for 5 min. The mixture was partitioned between ethyl acetate and water, and the organic phase washed with dilute acid, dried and evaporated, giving N^S-cyclohexyl-N^O-phenyl(thio-oxamide) (2·0 g., 86%), needles (from ethanol), m. p. and mixed m. p. 130°. The aqueous extract was shown to contain considerable amounts of thiosulphate by qualitative tests with acids, silver nitrate, and barium chloride.

(*b*) The sodium salt (3·28 g., 11·4 mmoles) was heated with cyclohexylamine as in (*a*). The mixture was partitioned between ethyl acetate (50 ml.) and water (20 ml.), and the ethyl acetate was then washed twice with water (2 × 10 ml.). The combined aqueous extracts were extracted twice with ether; dissolved ether was removed under reduced pressure, and the aqueous solution made up to 50 ml. This solution was analysed for sulphide, sulphite, and thiosulphate, as outlined by Mitchell and Ward.[20] The amounts of these three anions, expressed as mg.-atoms of S, were 0·3, 4·0, and 7·2 respectively. N^S-Cyclohexyl-N^O-phenyl(thio-oxamide) (2·53 g., 84·5%) was isolated from the ethyl acetate extract. Under the conditions of estimation, unchanged Bunte salt in the aqueous solution did not interfere.

(iii) A sample of cyclohexylammonium phenylcarbamoylmethyl thiolsulphate was heated at 140° for 5 min. Crystallisation of the molten mass from ethanol gave N^S-cyclohexyl-N^O-phenyl-(thio-oxamide), m. p. 130°.

Conversion of Sodium Phenylcarbamoylmethyl [^{35}S]Thiolsulphate into N^S*-Cyclohexyl-*N^O*-phenyl-(thio-oxamide).*—Aluminium discs (25 mm. diam., 4 mm. thick, 1 cm.^{3} well) were used for mounting radioactive samples, which were counted at infinite thickness by a thin-end Geiger-Müller tube (EHM 2^S) with a conventional scaler unit.

Sodium phenylcarbamoylmethyl thiolsulphate (0·25 g.) was dissolved in an ammoniacal solution of ammonium [^{35}S]sulphite (10 ml.; 2 μc/ml.) which had been adjusted to pH 8 by addition of acetic acid. After 2 days at room temperature, the solution was freeze-dried and ammonium acetate and sulphite were removed by vacuum-sublimation. The residue crystallised from ethanol–ether, and the labelled Bunte salt was heated at 70°/0·1 mm. until constant radioactivity was obtained. An average figure of 3450 c.p.m. was obtained.

The Bunte salt was then converted into N^S-cyclohexyl-N^O-phenyl(thio-oxamide) by cyclohexylamine as described in (ii*a*). The thio-oxamide was separated from inorganic material by the method outlined in (ii*b*). The aqueous solution was freeze-dried: the residue had an activity of 4960 c.p.m. After crystallisation from aqueous ethanol, the thio-oxamide gave 760 c.p.m., which fell to 740 c.p.m. after a second crystallisation.

Oxidation of N^O*-Cyclohexyl-*N^S*-phenyl(thio-oxamide).*—40% Peracetic acid (2 ml.) was added to a solution of the thio-oxamide (0·4 g.) in acetic acid (4 ml.). The yellow colour was instantly discharged. Water was added, and the precipitate was filtered off and crystallised from 2-methoxyethanol. *N*-Cyclohexyl-*N'*-phenyloxamide separated as needles, m. p. 205° (lit.,[21] 209°).

N-Phenyl-α-thio-oxamoylmorpholine.—Sodium phenylcarbamoylmethyl thiolsulphate (0·5 g.) and morpholine (3 ml.) were heated under reflux for 3 min. The *thioamide* (0·30 g., 68%) crystallised from methanol as pale yellow prisms, m. p. 166° (Found: C, 57·6; H, 5·6; S, 12·8. $C_{12}H_{14}O_2N_2S$ requires C, 57·6; H, 5·6; S, 12·8%). The m. p. was considerably depressed on admixture with a sample of di(phenylcarbamoylmethyl) disulphide, m. p. 164°.

NN'-Diphenyl(thio-oxamide) (*Monothio-oxanilide*).—The last-named salt (5 g.) was heated with aniline (10 ml.) at 160° for 15 min. The mixture was poured into water and extracted with ethyl acetate. This extract was washed with dilute acid, dried, and evaporated. A solution of the residue (1·6 g.) in benzene (100 ml.) was passed through a column of alumina, an orange band of impurities being retained at the top of the column. The eluate was evaporated to small volume, and light petroleum added, whereupon the thioamide (0·90 g., 21%) separated as yellow needles, m. p. 142°. Recrystallisation from ethanol raised the m. p. to 143·5° (lit.,[22] m. p. 143—144°). Found: C, 66·0; H, 4·7; N, 10·5; S, 12·2. Calc. for $C_{14}H_{12}ON_2S$: C, 65·6; H, 4·7; N, 10·9; S, 11·9%).

Oxidation with peracetic acid gave oxanilide as plates, m. p. and mixed m. p. 245°.

[20] Mitchell and Ward, "Modern Methods in Quantitative Chemical Analysis," Longmans, Green & Co., London, 1932, p. 138.
[21] de Vries, *Rec. Trav. chim.*, 1942, **61**, 223.
[22] Frerichs and Wildt, *Annalen*, 1908, **360**, 105.

N^S-*Allyl*-N^O-*phenyl*(*thio-oxamide*).—The last-named salt (1·5 g.) and allylamine (5 ml.) were heated under reflux on a steam-bath for 30 min. The product (0·48 g.) was chromatographed in benzene on alumina. The eluate contained the *thioamide*, m. p. 83° (from light petroleum) (Found: C, 60·1; H, 5·3; S, 14·4. $C_{11}H_{12}ON_2S$ requires C, 60·0; H, 5·5; S, 14·5%).

Oxidation of the thioamide with peracetic acid in the usual way gave N-*allyl*-N′-*phenyloxamide* as needles, m. p. 142° (from aqueous methanol) (Found: C, 64·9; H, 5·7. $C_{11}H_{12}O_2N_2$ requires C, 64·7; H, 5·9%).

Reaction of Sodium Phenylcarbamoylmethyl Thiolsulphate with Aqueous Amine Solutions.—(i) Aniline (0·6 ml.) was heated with the salt (1·0 g.) in water (20 ml.) on a steam-bath for 30 min. The precipitate (0·05 g.) was collected, and crystallised from aqueous methanol as needles, m. p. 161° undepressed on admixture with a sample of di(phenylcarbamoylmethyl) disulphide.

Addition of acetic acid (0·5 ml.) to the aqueous filtrate gave a precipitate (0·7 g.) of aniline (phenylcarbamoylmethyl) thiolsulphate, m. p. 177°.

(ii) Morpholine (1 ml.) was added to a solution of the Bunte salt (1·0 g.) in water (15 ml.). An immediate white precipitate separated. The mixture was heated on a steam-bath for a few minutes, then cooled and filtered. Crystallisation of the residue (0·52 g.) from methanol gave di(phenylcarbamoylmethyl) disulphide, m. p. 161°.

Reaction of Sodium Phenylcarbamoylmethyl Thiolsulphate with Potassium Cyanide.—Potassium cyanide (3 g.) was added to a solution of the salt (5·0 g.) in boiling water (50 ml.), and the solution allowed to cool spontaneously. Extraction with ethyl acetate gave 3-phenylpseudothiohydantoin (0·9 g.), m. p. 148° (from aqueous ethanol). The m. p. was considerably depressed on admixture with (phenylcarbamoylmethyl) thiolcarbamate, m. p. 147—148° (lit.,[23] m. p. 147°). Heating the product at 160° for 5 min. gave 2-phenyliminothiazolid-4-one, m. p. 177° (lit.,[17] m. p. 178°) (from ethyl acetate–light petroleum).

Reaction of 3-Phenylpseudothiohydantoin with Cyclohexylamine.—3-Phenylpseudothiohydantoin (0·5 g.) and cyclohexylamine (3 ml.) were heated under reflux for 10 min., then acidified and extracted with ethyl acetate. Evaporation of the extract gave a residue (0·15 g., 23%) which after two crystallisations from aqueous ethanol had m. p. 131°, undepressed on admixture with N^S-cyclohexyl-N^O-phenyl(thio-oxamide).

Reaction of phenylcarbamoylmethyl thiolcarbamate (2·0 g.) with cyclohexylamine (6 ml.) in the same way also gave N^S-cyclohexyl-N^O-phenyl(thio-oxamide) (0·15 g., 5%).

Sodium Cyclohexylcarbamoylmethyl Thiolsulphate.—This compound was obtained in 80% yield by reaction of chloroacetylcyclohexylamine with sodium thiosulphate in the usual way. The mixture was evaporated to dryness under reduced pressure and the residue was extracted with boiling ethanol from which the *product* was precipitated with ether (Found: C, 33·3; H, 5·6; N, 4·5; S, 21·4. $C_8H_{14}O_4NS_2Na,H_2O$ requires C, 32·8; H, 5·5; N, 4·8; S, 21·8%).

Di(*cyclohexylcarbamoylmethyl*) *Disulphide.*—Excess of aqueous iodine–potassium iodide was added to a concentrated aqueous solution of the last-mentioned thiolsulphate at 100°. After 5 min. the excess of iodine was discharged with sodium thiosulphate, and the *disulphide* filtered off and crystallised from aqueous ethanol. Colourless needles, m. p. 165°, were obtained (Found: N, 8·1; S, 18·4. $C_{16}H_{28}O_2N_2S_2$ requires N, 8·1; S, 18·6%).

NN′-*Dicyclohexyl*(*thio-oxamide*).—The last-mentioned thiolsulphate (1·0 g.) was heated under reflux with cyclohexylamine (3 ml.) for 5 min., and the product precipitated by acid. The *thioamide* (0·95 g., 95%) crystallised from ethanol as yellow plates, m. p. 165° (Found: N, 10·0; S, 11·7. $C_{14}H_{24}ON_2S$ requires N, 10·4; S, 11·9%). The m. p. was considerably depressed on admixture with a sample of di(cyclohexylcarbamoylmethyl) disulphide.

With peracetic acid the thioamide gave *NN′*-dicyclohexyloxamide, m. p. 273° (lit.,[21] m. p. 273°).

Reaction of Sodium Cyclohexylcarbamoylmethyl Thiolsulphate with Aqueous Ammonia.—A solution of the thiolsulphate (1 g.) in 5% aqueous ammonia (15 ml.), was boiled for several minutes, then cooled and the precipitate was collected. Crystallisation from ethanol gave a small crop of colourless plates, m. p. 225°, raised to 228° by a second crystallisation. The m. p. was undepressed on admixture with *N*-cyclohexyloxamide (lit.,[21] m. p. 234°; see below).

Addition of water to the mother-liquor gave a substantial precipitate from which di(cyclohexylcarbamoylmethyl) disulphide, m. p. 154°, was obtained by crystallisation from aqueous ethanol.

Sodium Carbamoylmethyl Thiolsulphate.—This compound was prepared from chloroacetamide and sodium thiosulphate in the usual way. It could not be extracted from the residue

[23] Beckurts and Frerichs, *J. prakt. Chem.*, 1902, **66**, 181.

with hot ethanol, nor would it crystallise from water, and the crude mixture of Bunte salt and sodium chloride was used as such. On addition of a solution of *S*-benzylthiuronium chloride to an aqueous solution, a precipitate of *S-benzylthiuronium carbamoylmethyl thiolsulphate* separated. It crystallised from water as needles, m. p. 138° (Found: S, 28·5. $C_{10}H_{15}O_4N_3S_3$ requires S, 28·5%).

N^8-*Cyclohexyl(thio-oxamide)*.—A suspension of the crude Bunte salt in cyclohexylamine was heated under reflux for 10 min. The product was chromatographed in benzene on alumina. The *thioamide* was eluted with ether–benzene (1 : 4); it crystallised from light petroleum as yellow laths, m. p. 108° (Found: C, 52·1; H, 7·7; N, 14·6; S, 17·3. $C_8H_{14}ON_2S$ requires C, 51·6; H, 7·5; N, 15·1; S, 17·2%).

Oxidation with peracetic acid gave *N*-cyclohexyloxamide as needles, m. p. 230° (from 2-methoxyethanol).

N^8-*Phenyl(thio-oxamide)*.—Reaction of the crude Bunte salt with aniline at 160° for 10 min. gave a product from which N^8-phenyl(thio-oxamide), m. p. 167° (lit.,[2] 169°), was obtained by chromatography on alumina followed by crystallisation from ethanol.

Oxidation with potassium ferricyanide in alkaline solution gave benzothiazole-2-carboxyamide as plates, m. p. 238° (lit.,[2] 238—240°).

Cyclohexylammonium Benzyl Thiolsulphate.—Cyclohexylamine (2 ml.) was added to a warm solution of sodium benzyl thiolsulphate (5 g.) in water (50 ml.) containing acetic acid (2 ml.). A small quantity (0·5 g.) of oil separated, and the aqueous phase was decanted. The oil crystallised from ethanol as needles, m. p. 68°, undepressed on admixture with dibenzyl disulphide. Cooling the aqueous phase deposited crystals. These were filtered off, and recrystallised (3·6 g.) from water. The *cyclohexylammonium salt* was obtained as needles, m. p. 137° (Found: C, 51·6; H, 7·0. $C_{13}H_{21}O_3NS_2$ requires C, 51·5; H, 7·0%).

A sample of the salt was heated at 140° for 10 min. Crystallisation of the melt from methanol gave dibenzyl disulphide, m. p. 70°.

Reaction of Sodium Benzyl Thiolsulphate with Amines.—(i) A solution of the thiolsulphate (1·0 g.) and cyclohexylamine (2 ml.) in water (25 ml.) was heated on a steam-bath for 10 min., then extracted with ethyl acetate, and the extracts were washed with dilute hydrochloric acid and dried. Evaporation gave dibenzyl disulphide (0·24 g., 44%). The aqueous phase was acidified, and extracted with ethyl acetate. This extract gave an oil (0·11 g.).

(ii) A suspension of the thiolsulphate (2·0 g.) in morpholine (3 ml.) was heated under reflux for 5 min. Dilute hydrochloric acid was added to the cold mixture, and the precipitate (0·8 g.) filtered off. Crystallisation from methanol gave dibenzyl disulphide, m. p. 68°.

(iii) A similar experiment with cyclohexylamine instead of morpholine also gave dibenzyl disulphide.

(iv) The thiolsulphate (5·6 g.), sulphur (3·2 g.), and morpholine (10 ml.) were heated under reflux for 15 min. The neutral product (4·67 g.) gave thiobenzomorpholide (3·45 g., 67%) as pale yellow prisms, m. p. 137° (from methanol).

Reaction of Sodium o-Nitrophenyl Thiolsulphate with Amines.—Sodium *o*-nitrophenyl thiolsulphate was prepared by reaction of *o*-nitrobenzenesulphenyl chloride with sodium sulphite as described by Lecher and Hardy.[24]

(i) The Bunte salt (1·0 g.) was heated with aniline (2 ml.) at 140° for 10 min. On addition of dilute hydrochloric acid to the cold mixture, di-*o*-nitrophenyl disulphide (0·49 g., 85%) was precipitated.

(ii) Reaction of the Bunte salt with cyclohexylamine under similar conditions also gave the disulphide.

Attempted Reaction of Potassium Phenyl Thiolsulphate with Amines.—Potassium phenyl thiolsulphate was prepared by reaction of diphenyl disulphide with potassium sulphite.[24]

Heating it with cyclohexylamine or aniline at 140°, or with aqueous cyclohexylamine at 100°, did not result in reaction, the Bunte salt being recovered unchanged in each case.

Reaction of Sodium 2-(Phenylcarbamoyl)ethyl Thiolsulphate with Amines.—This Bunte salt was prepared from the corresponding chloro-compound as described by Weiss and Sokol.[19] Reaction with cyclohexylamine or morpholine at 135° for 10 min. gave a product from which unchanged Bunte salt (70%) and di-(2-phenylcarbamoylethyl) disulphide (20%) were isolated.

DIVISION OF PROTEIN CHEMISTRY (FORMERLY BIOCHEMISTRY UNIT),
COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION,
MELBOURNE, AUSTRALIA. [*Received, February 16th*, 1959.]

[24] Lecher and Hardy, *J. Org. Chem.*, 1955, **20**, 475.

595. *The Kinetics of the Oxidation of Some Bipyridyl and Phenanthroline Complex Ions by the Peroxydisulphate Ion in Aqueous Solution.*

By D. H. Irvine.

The kinetics of the oxidation of the tris-2,2′- and tris-4,4′-dimethylbipyridylium(II), tris-αα′-bipyridylruthenium(II), tris-*o*-phenanthrolineiron(II), and tris-5-methylphenanthrolineiron(II) ions by the peroxydisulphate ion in aqueous solution have been studied at different temperatures under varying conditions of ionic strength. The rates of the reactions increase as the standard redox potential difference between the peroxydisulphate and complex ion couples increases, the velocity constants being well represented by the equation, $\log_{10} k_0 = \text{Constant} + x\,\Delta E^0$, x being ~7·0. Similar equations are applicable to other redox systems.

Marcus [1] concluded that the factors which are important in determining the speed of electron-transfer reactions are (1) the standard free-energy change of the redox step, (2) the Coulombic interaction of the ionic charges of the reactants, and (3) the solvation of the charged reactants. Solvation effects will account to some extent for the difference in rates between electron-transfer reactions involving simple aquated ions on the one hand and complex ions on the other, and in some cases must be the predominant factor, *e.g.*, in the fast exchange between $Fe(CN)_6^{4-}$ and $Fe(CN)_6^{3-}$ compared with that between Fe^{2+} and Fe^{3+}. Coulombic interaction is known to affect markedly the rate of an ionic reaction, and in some cases a simple relation exists between the product of the charges of the reactants and the A factor in the Arrhenius equation.[2] However, its relative importance in redox reactions is uncertain. A number of electron-transfer reactions have been shown to be fast despite the adverse nature of Coulombic interaction.

For (1), there are some isolated examples which suggest that this factor, or the overall free-energy change, is of some importance in determining the rate of a redox reaction. George and Irvine [3] suggest that it is the overall free-energy change which probably accounts for the difference between the rate of oxidation of the trisbipyridylruthenium(II) ion by ceric ion in aqueous perchloric acid on the one hand and that in aqueous sulphuric acid on the other. A similar suggestion has been made concerning the rates of oxidation of the trisbipyridylosmium(II) and tris-*o*-phenanthrolineiron(II) ions by thallic ion in aqueous perchloric acid.[4] Marcus [1] attributes the different rates of oxidation of some substituted quinols by ferric ion to the different free energies of the rate-determining step. Here, however, the assumption has to be made that the rate-determining step in all these reactions is the same, *viz.*, $Fe^{3+} + HQ^- \rightleftharpoons Fe^{2+} + HQ$, where HQ^- is the anion of the quinol. This may or may not be so, since the data are equally consistent with hydrogen-atom transfer and there is no way of deciding which mechanism operates in any given reaction.

In an attempt to establish unequivocally the importance of the standard free-energy change as a factor in determining the rate of a redox reaction, the kinetics of the oxidation of the complex ions, *viz.*, tris-4,4′-dimethylbipyridyliron(II), tris-αα′-bipyridyliron(II), tris-*o*-phenanthrolineiron(II), tris-5-methylphenanthrolineiron(II), and tris-αα′-bipyridylruthenium(II) by the peroxydisulphate ion were investigated. These ions each have roughly the same partial molal entropies in their reduced and oxidized forms,[5] so that solvation effects will affect their rates of oxidation to approximately the same extent. Further, being all bivalent ions, as is known from the effect of ionic strength on the redox potential of the M^{II}—M^{III} couples and confirmed in these experiments by the effect of

[1] Marcus, *J. Chem. Phys.*, 1957, **26**, 867.
[2] Glasstone, Laidler, and Eyring, "Theory of Rate Processes," McGraw-Hill, New York, 1941.
[3] George and Irvine, *J.*, 1954, 857.
[4] Irvine, *J.*, 1957, 1841.
[5] George, Hanania, and Irvine, unpublished work.

XUM

ionic strength on their rates of oxidation, coulombic interaction affects each system in the same way. Any difference, therefore, in the rates of oxidation of these ions by $S_2O_8^{2-}$ can probably be attributed to the different free-energy changes of the reactions. The latter are directly related to the standard redox potentials of the M^{2+}—M^{3+} couples, which vary from 0·941 v for the tris-4,4′-dimethylbipyridyliron$^{2+/3+}$ couple to 1·374 v for the tris-αα′-rutheniumbipyridyl$^{2+/3+}$ couple.

The results recorded in this paper show that there is a direct relation between the rate and the standard free energy of a redox reaction.

Kinetics.—As in the oxidation of the trisdipyridylosmium(II) ion,[6] the oxidation of the tris-4,4′-dimethylbipyridyliron(II) ion by $S_2O_8^{2-}$ initially followed second-order kinetics, consistent with the equation

$$k = \frac{2{\cdot}303}{t(b-2a)} \log_{10} \frac{a(b-2x)}{b(a-x)}$$

where a is the initial concentration of $S_2O_8^{2-}$, b the initial concentration of the complex ion, and x the amount of $S_2O_8^{2-}$ used up in time t. Departure from second-order kinetics occurred after about 30—40% reaction, no doubt mainly for the same reason as that

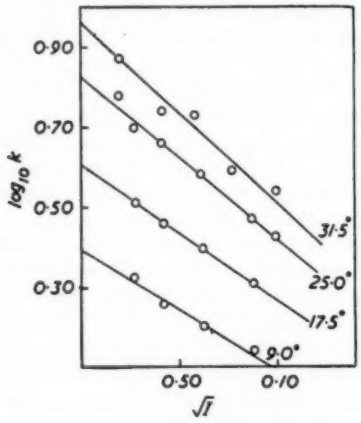


FIG. 1. Log_{10} *k versus* $\sqrt{I}$ *plots for the reaction between tris-4,4′-dimethylbipyridyliron*(II) *ion and* $S_2O_8^{2-}$.

proposed for the trisdipyridylosmium(II) system. However, there is the further factor in this case that the oxidised form of the complex ion, as with other bipyridyl and phenanthroline complexes of iron, is not stable under the conditions of the experiment.

The rate of the reaction was measured at 9·0°, 17·5°, 25·0°, and 31·5° under varying conditions of ionic strength. The results are illustrated in Fig. 1 where $\log_{10} k$ is plotted against $\sqrt{I}$. The slopes of the lines are 3·30, 3·40, 3·75, and 4·20 at 9·0°, 17·5°, 25·0°, and 31·5° respectively. These are in fair agreement with the theoretical slope of 4·0 expected for a reaction between oppositely charged bivalent ions. Extrapolation of the $\sqrt{I}$ plot to zero ionic strength gives values of k_0, the true velocity constant, of 2·50, 4·00, 6·68, and 9·34 l. mole^{-1} sec.$^{-1}$ at 9·0°, 17·5°, 25·0°, and 31·5°, respectively. A plot of $\log_{10} k_0$ against $1/T$ yields:

$$k_0 = 3{\cdot}2 \times 10^8 \exp(-10{,}600/RT) \quad \ldots\ldots (1)$$

Similar kinetic behaviour was observed in the oxidation of the tris-αα′-bipyridyliron(II), tris-*o*-phenanthrolineiron(II) and tris-5-methylphenanthrolineiron(II) ions. These reactions were followed under conditions where pseudo-first-order kinetics applied and departure from such kinetics was observed between 20 and 30% reaction. The oxidation of tris-αα′-bipyridylruthenium(II) ion was found, somewhat unexpectedly, to be catalysed by sunlight. However, in the absence of sunlight reproducible kinetics were obtained.

[6] Irvine, *J.*, 1958, 2166.

As in the case of the tris-4,4′-dimethylbipyridyliron(II) ion all the reactions were studied under varying conditions of ionic strength and at different temperatures. In all cases, except that of the tris-5-methylphenanthrolineiron(II) ion, the perchlorates of the complex ions were used. The perchlorate of tris-5-methylphenanthrolineiron(II) was, however, too insoluble, and a solution of the sulphate was used. Since the concentration of complex ion was of the order of 5×10^{-5}M no appreciable catalysis of the rate by sulphate ion [6] was expected.

The results are summarised in Table 1. In each case the A factor is low for a reaction between oppositely charged ions but is nevertheless much the same as that for the similar reaction between $Os(dipy)_3^{2+}$ and $S_2O_8^{2-}$. The slopes of $\sqrt{I}$ plots in the tris-αα′-bipyridylruthenium(II) system are much less than expected but there is no real reason to believe that the mechanism of the reaction differs from that for the others.

TABLE 1.

Complex ion	Temp.	Slope ($\sqrt{I}$ plot)	$10k_0$ (l. mole^{-1} sec.$^{-1}$)	10^3A	E (kcal. mole^{-1})
Tris-αα′-dipyridyliron(II) ...	11·5°	3·80	2·29		
	19·6	3·70	3·72	5·7	12,400
	25·5	4·05	5·70		
	32·2	4·10	9·12		
Tris-*o*-phenanthrolineiron(II)	19·5	3·70	1·95		
	26·5	3·05	3·05	15·0	13,300
	33·0	3·50	5·25		
Tris-5-methylphenanthroline-iron(II)	17·0	3·6	1·12		
	33·0	3·0	1·30	1·6	12,600
Tris-αα′-bipyridylruthen-ium(II)	26·5	2·5 *	0·105		
	32·0	2·6 *	0·155	5·0	14,600
	40·0	2·5 *	0·282		

* $\log_{10} k$ plotted against $[\sqrt{I}/(1 + \sqrt{I})]$

Relation between the Rates and Standard Free-energy Changes.—The rates of oxidation of the trisbipyridylosmium(II) ion as well as of the tris-4,4′-dimethylbipyridyliron(II) ion, which are consistent with the oxidation of 2 mols. of the bivalent complex ion by 1 mole of $S_2O_8^{2-}$, suggest that the overall oxidation can be represented:

$$2M^{2+} + S_2O_8^{2-} \rightleftharpoons 2M^{3+} + 2SO_4^{2-} \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where M^{2+} and M^{3+} represent respectively the bivalent complex ion and its oxidation product. The standard free-energy change corresponding to equation (2) is given by

$$\begin{aligned} \Delta G^0 &= -2F[E^0(S_2O_8^{2-}) - E^0(\text{complex})] \\ &= -2F\Delta E^0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3) \end{aligned}$$

where $E^0(S_2O_8)$ is the standard redox potential of the SO_4^{2-}–$S_2O_8^{2-}$ couple and is 2·01 v (see ref. 13) and E^0 (complex) that of the M^{2+}–M^{3+} couple. If the rates and standard free-energy changes of the above reactions are related, it follows from equation (3) that a similar relation exists between the rates and ΔE^0 values for these reactions. Table 2 shows the results for reactions at 25°, with those for trisbipyridylosmium(II) for comparison. E^0 values for the trisbipyridylosmium$^{2+/3+}$, tris-αα′-bipyridyliron$^{2+/3+}$, tris-*o*-phenanthroline-iron$^{2+/3+}$, and tris-αα′-bipyridylruthenium$^{2+/3+}$ couples are those from the work of Barnes, Dwyer, and Gyarfas,[7] and of George, Hanania, and Irvine.[5] The value for the tris-5-methylphenanthrolineiron$^{2+/3+}$ couple is estimated from the value of 1·06 v in 0·1M-sulphuric acid.[8] That for the tris-4,4′-dimethylbipyridyliron$^{2+/3+}$ couple was determined in this investigation. The results of the experiments are recorded below.

A plot of $\log_{10} k_0$ against ΔE^0 is shown in Fig. 2. Its linearity indicates a direct relation between the rates of these reactions and their standard free-energy changes. The evidence, however, does not distinguish whether it is the overall free-energy change or that of the rate-determining step which is significant, for in these systems where there is a common

[7] Barnes, Dwyer, and Gyarfas, *Trans. Faraday Soc.*, 1952, **48**, 269.
[8] Brandt and Smith, *Analyt. Chem.*, 1949, **21**, 1313.

TABLE 2. *Effect of ΔE^0 on the rate of oxidation of some bipyridyl and phenanthroline complex ions by $S_2O_8^{2-}$.*

Complexion	ΔE^0	k_0 (l. mole^{-1} sec.$^{-1}$) (25°)	Complexion	ΔE^0	k_0 (l. mole^{-1} sec.$^{-1}$) (25°)
$Os(bipy)_3^{2+}$	1·13	49·0	$Fe(o\text{-phen})_3^{2+}$	0·87	0·30
$Fe(4,4\text{-}Me_2\text{-bipy})_3^{2+}$	1·07	6·68	$Fe(5\text{-Me-phen})_3^{2+}$	~0·86	0·11
$Fe(bipy)_3^{2+}$	0·89	0·55	$Ru(bipy)_3^{2+}$	0·64	0·009

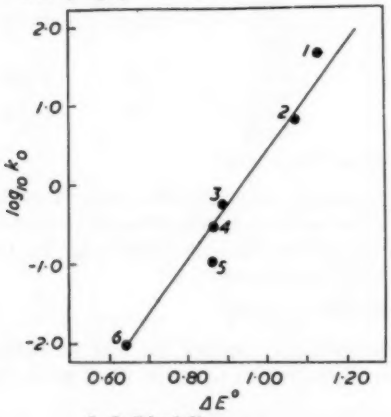
mechanism the two are directly related. The straight line in Fig. 2 can be represented by the equation,

$$\log_{10} k_0 = -6{\cdot}4 + x\Delta E^0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where $x \approx 7{\cdot}0$.

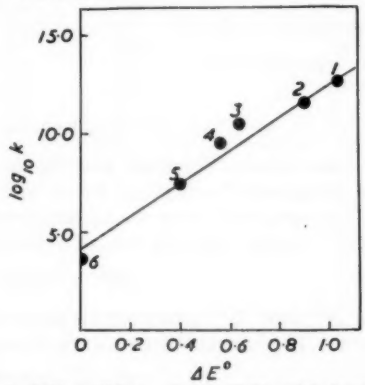
Consideration of other redox systems in the literature, where the reaction mechanisms are similar and both solvation and charge effects are comparable, shows that an equation similar to (4) also fits the data for these systems. Thus in Fig. 3 the values of $\log_{10} k$ for the reactions between Fe^{3+} and HQ^-,[9] Fe^{3+} and substituted HQ^-,[10] Fe^{3+} and HO_2^-,[11] and

FIG. 2. *Relation between the rates of oxidation of some bipyridyl and phenanthroline complex ions by $S_2O_8^{2-}$ and ΔE^0.*



1, $Os(bipy)_3^{2+}$.
2, $Fe(4,4'\text{-}Me_2\text{-bipy})_3^{2+}$.
3, $Fe(bipy)_3^{2+}$.
4, $Fe(o\text{-phen})_3^{2+}$.
5, $Fe(5\text{-Me-phen})_3^{2+}$.
6, $Ru(bipy)_3^{2+}$.

FIG. 3. *Relation between the rates of oxidation of some HX^- ions by Fe^{3+}, Co^{3+}, and ΔE^0.*



1, $Co^{3+} + HO_2^-$. 2—6, Fe^{3+} with ions from (2) duroquinol, (3) toluquinol, (4) quinol, and (5) 2,6-dichloroquinol, and with (6) HO_2^-.

Co^{3+} and HO_2^- [12] are plotted against ΔE^0. ΔE^0 for the last two reactions are estimated from Latimer's values [13] to be approximately zero and 1·05 v respectively. ΔE^0 for the Fe^{3+}–HQ^- reactions are calculated from the values of ΔG^0 quoted by Marcus.[1] The straight-line plot in this equation is approximately represented by the equation

$$\log_{10} k = 4{\cdot}0 + 9{\cdot}0\Delta E^0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The idea that a relation exists between the rate of a redox reaction and its standard free-energy change is not new. Barron [14] showed that a plot of the logarithm of the time

[9] Baxendale, Hardy, and Sutcliffe, *Trans. Faraday Soc.*, 1957, **47**, 963.
[10] Baxendale and Hardy, *ibid.*, 1954, **50**, 808.
[11] Barb, Baxendale, George, and Hargrave, *ibid.*, 1951, **47**, 491.
[12] Baxendale, "Kinetics and Mechanism of Inorganic Reactions in Solutions," *Chem. Soc. Special Publ.* No. 1, London, 1954, p. 43.
[13] Latimer, "Oxidation Potentials," 2nd edn., Prentice-Hall, New York, 1952.
[14] Barron, *J. Biol. Chem.*, 1932, **97**, 287.

required to attain 50% autoxidation of a number of similar leuco-dyes against E^0 for the dye couple is linear. Bolland and Ten Have,[15] in studying the inhibitory effects of phenolic compounds on the thermal oxidation of ethyl linoleate, found similarly that the logarithm of the relative efficiency of inhibition, which is directly related to the chain-termination between RO_2 and the phenol, varies directly with E^0 for the phenol couple. These and the above examples seem to indicate that the relation is general for redox reactions. The relation is particularly useful since it enables one to predict the rate of a given redox reaction once the rates of similar reactions are known. On the other hand, it may be used to confirm the mechanism of a given reaction once the rate of the reaction has been established.

Measurement of E^0 for the Tris-4,4′-dimethylbipyridyliron(II)*–tris-4,4′-dimethylbipyridyliron*(III) *Couple.*—The redox potential of this couple was measured at different ionic strengths and temperatures. At 25° E varied with ionic strength according to the equation, $E = 0{\cdot}941 - 0{\cdot}20\ [\sqrt{I}/(1 + \sqrt{I})]$. The slope of this line is in fair agreement with the theoretical slope of −0·15 for a couple in which there is a charge of +2 on the reduced and +3 on the oxidized form. At constant I (0·105) the values of E at 15·0°, 25·0°, and 33·5° were 0·927, 0·920, and 0·913 v respectively. dE/dT is thus −0·00075 v per degree. For the reaction

$$Fe(4,4'\text{-Me-bipy})_3^{3+} + \tfrac{1}{2}H_2 \rightleftharpoons Fe(4,4'\text{-Me-bipy})_3^{2+} + H^+$$

$\Delta G^0 = -21{\cdot}6$ kcal./mole, $\Delta H = -26{\cdot}8$ kcal./mole, and $\Delta S^0 = -17{\cdot}5$ e.u.; $\bar{S}^0_{red.} - \bar{S}^0_{ox.}$ is therefore −1·9 e.u. ($\bar{S}^0$ for H^+ being assumed to be zero), which is of the same order of magnitude as $\bar{S}^0_{red.} - \bar{S}^0_{ox.}$ for other bipyridyl and phenanthroline complexes.[5]

Experimental

Materials.—Solutions of tris-4,4′-dimethylbipyridyliron(II), tris-αα′-bipyridyliron(II), and tris-*o*-phenanthrolineiron(II) were prepared from weighed amounts of the perchlorate salts. The latter were obtained by addition of a solution of sodium perchlorate to the sulphate solutions. Tris-αα′-bipyridylruthenium(II) perchlorate was precipitated from a solution of tris-αα′-bipyridylruthenium(II) chloride hexahydrate. The chloride was obtained from the G. Fredrick Smith Chemical Company. The perchlorate of tris-5-methylphenanthrolineiron(II) was too insoluble for use and a solution of the sulphate was used instead. This was prepared by adding exactly three equivalents of 5-methylphenanthroline to one of " AnalaR " ferrous ammonium sulphate and making up to the appropriate volume.

The preparation of sodium perchlorate solution has already been described, as well as the conductivity water used in these experiments.[4,6] " AnalaR " potassium peroxydisulphate was used without purification.

Rate Measurements.—The reactions were followed spectrophotometrically at the wavelength maxima of the complex ions. In all cases the oxidized forms had negligible absorption. Duplicate runs agreed to within 5%.

E.M.F. Measurements.—The apparatus used has already been described.[16] The method was that of adding the appropriate amount of standard ceric sulphate solution to the complex ion to give an approximately equimolar mixture of the reduced and the oxidized form, and then determining simultaneously the E.M.F. potentiometrically and the concentrations of reduced and oxidized forms spectrophotometrically. The concentration of complex ion was $\sim 10^{-3}$M for E.M.F. and 10^{-4}M for spectrophotometric measurements. A Unicam Quartz spectrophotometer was used. Ionic strength was varied by the addition of " AnalaR " sodium nitrate.

I thank Mr. S. A. Olaitan for his help with the E.M.F. measurements.

Department of Chemistry, University College,
Ibadan, Nigeria. [*Received, March 9th*, 1959.]

[15] Bolland and Ten Have, *Discuss. Faraday Soc.*, 1947, **2**, 252.
[16] George, Hanania, and Irvine, *J.*, 1957, 3048.

596. *The Activation of Carbon–Carbon Double Bonds by Cationic Catalysts. Part VIII.*[1] *Cyclisation of* 1 : 1 : 3 : 3-*Tetraphenylbut*-1-*ene.*

By Alwyn G. Evans and D. Price.

In previous Parts the dimerisation of 1 : 1-diphenylethylene was studied with various catalysts. In all cases so far examined the linear olefinic dimer, 1 : 1 : 3 : 3-tetraphenylbut-1-ene, was formed. The formation of a cyclic non-olefinic dimer, 3-methyl-1 : 1 : 3-triphenylindane, is possible, however, under certain conditions.[2] We have now examined the formation of this indane under rigorous high-vacuum conditions; its formation is associated with a very adverse entropy term.

Experimental

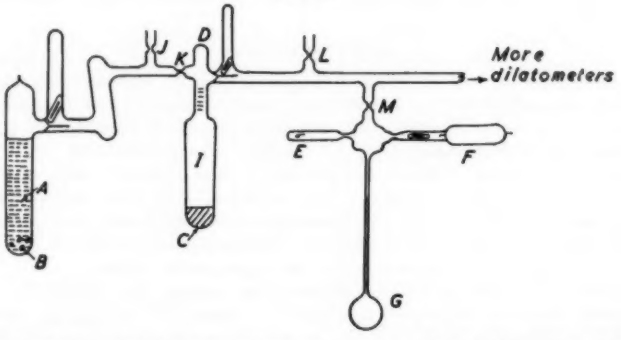
Materials.—Stannic chloride was prepared and purified as described in Part V.[3]

" AnalaR " benzene was purified by standard methods and then outgassed under high vacuum and distilled over a bright sodium film into a receiver (*A*, Fig. 1), where it was kept over sodium–potassium alloy, (*B*). Immediately before use the pure benzene was distilled off the alloy.

Hydrogen chloride was prepared by the action of " AnalaR " sulphuric acid on " AnalaR " ammonium chloride.[1]

1 : 1 : 3 : 3-Tetraphenylbut-1-ene (linear dimer, LD) was prepared by dissolving 200 g. of 1 : 1-diphenylethylene, freshly fractionated off potassium hydroxide, in 1500 ml. of " AnalaR "

Fig. 1.



benzene which had been dried over sodium wire. To this solution were added 25 ml. of anhydrous B.D.H. stannic chloride. The solution was then kept in a stoppered " Quickfit " flask for 7 days. It was then washed with water to remove all trace of catalyst, and the benzene pumped off to leave the crude 1 : 1 : 3 : 3-tetraphenylbut-1-ene. This was then recrystallised 4 or 5 times from absolute ethanol to give the pure product, m. p. 113° (lit.,[2] m. p. 113°).

3-Methyl-1 : 1 : 3-triphenylindane (cyclic dimer, CD), prepared according to Schoepfle and Ryan's method,[2] had m. p. 143° (lit.,[2] m. p. 143°).

Procedure.—Dilatometers were filled with known concentrations by means of the apparatus shown in Fig. 1. The calibrated vessel (*I*) was first baked out under high vacuum and then opened at the point *D* to allow the introduction of a known weight of 1 : 1 : 3 : 3-tetraphenylbut-1-ene (*C*). The apparatus was resealed at *D* and re-evacuated. This linear dimer was then degassed by alternately melting and solidifying it under high vacuum, and the apparatus was then sealed off at *J*. The vessel (*A*) containing the purified benzene was then opened to the system by operating the magnetic breaker, and the benzene distilled on the dimer (*C*) until the vessel was filled to the calibration scale. The vessel was then sealed off at the constriction

[1] Part VII, Evans and Lewis, *J.*, 1959, 1946.
[2] Schoepfle and Ryan, *J. Amer. Chem. Soc.*, 1930, **52**, 4021.
[3] Evans and Lewis, *J.*, 1957, 2975.

K; the dimer dissolved in the benzene and the solution became homogeneous. The volume was then measured on the scale at a known temperature.

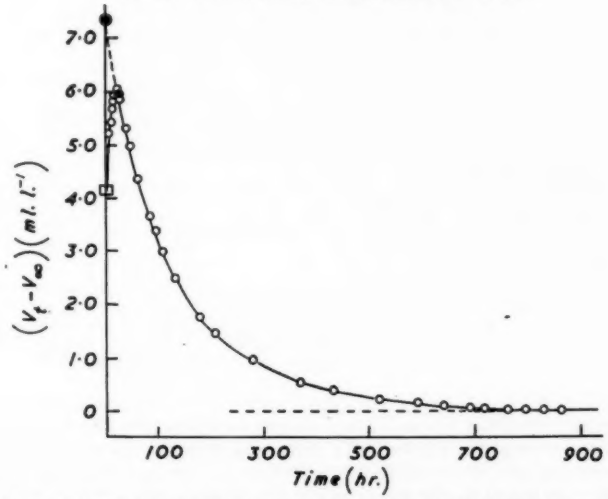
The vessel, *I*, was then sealed to the dilatometer system as shown. The whole apparatus was thoroughly evacuated and then sealed off at *L*. The linear dimer solution was then opened to the system by operating the magnetic breaker and each dilatometer was filled to a convenient point under vacuum. The dilatometer was then sealed off at *M*. Stannic chloride was introduced into the dilatometer by carefully exploding by heat the calibrated bulb in *E*, filled under high vacuum with a known volume of stannic chloride. The bulb *F* containing hydrogen chloride was then opened by operating the magnetic breaker and the gas frozen into the dilatometer bulb by use of liquid air. The dilatometer was then sealed off at the top of its stem while its bulb was still immersed in liquid air. The contents of the dilatometer were then allowed to melt and become homogeneous before the dilatometer was placed in a thermostat. The volume changes were followed in thermostats kept at 30·0°, 40·1°, and 54·9°.

The volume change involved in the conversion of 1 mole of the monomer into ½ mole of the cyclic dimer was found to be 17·2 ml. by determining the densities of solutions containing equal weights of the monomer or cyclic dimer in the same weights of benzene at the three temperatures. The volume changes from monomer to linear dimer have been determined previously.[3] The change from linear dimer to monomer involves an expansion, and that from linear dimer to cyclic dimer a contraction.

Two dilatometers, one containing linear dimer, stannic chloride, and benzene, but no hydrogen chloride, and the other cyclic dimer, stannic chloride, hydrogen chloride, and benzene, were used as blanks.

The product of the reaction (m. p. 143°) was extracted, and found to be the indane.

FIG. 2. *Volume change during reaction at 54·9°.*



$[SnCl_4] = 4·99 \times 10^{-2}$ mole l.$^{-1}$, $[HCl] = 1·03 \times 10^{-1}$ mole l.$^{-1}$, [Total CD] formed at $t_\infty = 4·603 \times 10^{-1}$ mole l.$^{-1}$.

□ Calculated initial point in terms of linear dimer.

● Calculated initial point in terms of monomer–linear dimer equilibrium mixture.

RESULTS

In order to obtain the cyclic dimer at a measurable rate much higher concentrations of stannic chloride and hydrogen chloride are required than those used for the monomer–linear dimer equilibration experiments.[1] Under these conditions of high catalyst concentration the monomer–linear dimer equilibrium is established very rapidly, and one measures the rate of production of the cyclic dimer from this equilibrium mixture of monomer and linear dimer. We therefore studied the reaction by starting with the linear dimer, and not with monomer

as in the previous Parts, since in this way we can observe the rapid establishment of the monomer–linear dimer equilibrium as an expansion, and the slower formation of cyclic dimer as a contraction. This is seen in the typical reaction plot in Fig. 2, where the initial expansion is over very quickly and the subsequent contraction occurs slowly, We have included on this curve two initial points, one calculated in terms of linear dimer, and the other in terms of monomer–linear dimer equilibrium mixture, this equilibrium being assumed to be established instantaneously. The broken portion of the curve shows how the volume change would have occurred if monomer–linear dimer equilibration had occurred immediately at zero time.

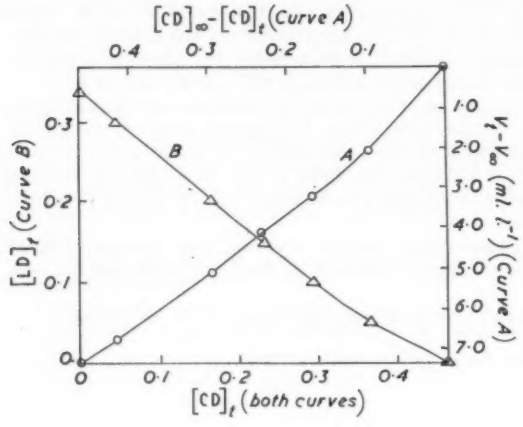


FIG. 3. *Calibration curves at* 54·9°.
[Total CD] formed at $t_\infty = 4{\cdot}603 \times 10^{-1}$ mole l.$^{-1}$.

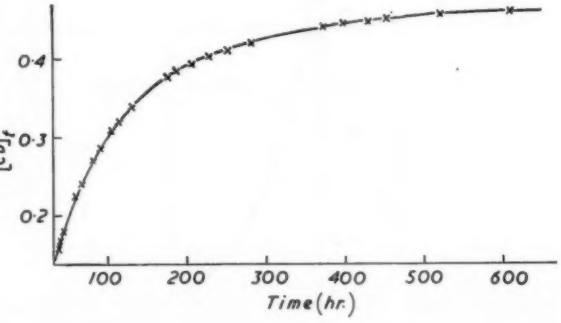


FIG. 4. *Change in* [CD] *during reaction at* 54·9°.
$[SnCl_4] = 4{\cdot}99 \times 10^{-2}$ mole l.$^{-1}$, $[HCl] = 1{\cdot}03 \times 10^{-1}$ mole l.$^{-1}$, [Total CD] formed at $t = 4{\cdot}603 \times 10^{-1}$ mole l.$^{-1}$.

The dilatometer containing linear dimer, stannic chloride, and benzene but no hydrogen chloride showed no change in volume with time and was colourless. This establishes the purity of the reagents and shows that the formation of cyclic dimer requires a cocatalyst. (In earlier papers [4] we found it difficult to purify the linear dimer when it was made from the monomer by catalysis with sulphuric acid. The present method of preparation gave very pure material.)

The dilatometer containing cyclic dimer, stannic chloride, benzene, and hydrogen chloride also showed no volume change with time and was colourless. This means that, unlike the formation of the monomer from the linear dimer, the formation of cyclic dimer is irreversible. Thus the asymptote to the curve in Fig. 2 represents total conversion into cyclic dimer. If the volume at any time t is V_t and that at infinite time is V_∞, a calibration curve for converting the quantity $(V_t - V_\infty)$ into the concentration of cyclic dimer still to be formed at time t is shown in Fig. 3, curve A. This curve also gives the relation between $(V_t - V_\infty)$ and the concentration of cyclic dimer at time t. A further calibration curve has been drawn relating

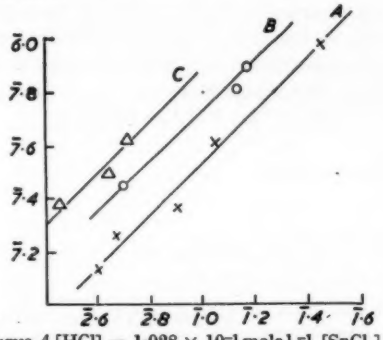
[4] (*a*) Evans, Jones, and Thomas, *J.*, 1955, 1824; (*b*) Evans, Jones, Jones, and Thomas, 1956, 2757.

the concentration of cyclic dimer at time t to the equilibrium concentration of linear dimer at time t (Fig. 3, curve B). All these curves are calculated from the volume changes for the complete conversion of one species into another and from the known equilibrium constants for the monomer–linear dimer equilibria.[1]

Using the calibration curve (Fig. 3, curve A), we have replotted that part of Fig. 2 to the right of the maximum as cyclic dimer concentration against time (Fig. 4) for all reactions. Tangents to this curve give values for the rate of formation of the cyclic dimer at this time (t) (since this reaction to cyclic dimer is irreversible it is not necessary, as in the monomer–linear dimer equilibration, to measure initial rates). The linear dimer concentration at time t is also known from the calibration curve (Fig. 3, curve B).

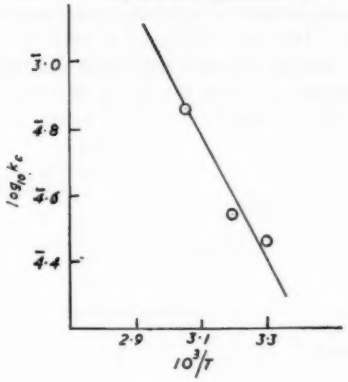
The order of reaction in linear dimer was found from the dependence of rate on [LD], (*a*) as a given reaction proceeds, and (*b*) from one reaction system to another, to be $1{\cdot}0 \pm 0{\cdot}1$ (Fig. 5).

FIG. 5. *Plots of* $\log_{10}$ (*Rate of formation of* CD) *at* 54·9° (*vertical axis*) *against* $\log_{10}$ [LD] *for curve A*, $\log_{10}$ [HCl] *for curve B*, log [$SnCl_4$] *for curve C.*



Curve A [HCl] = $1{\cdot}028 \times 10^{-1}$ mole l.$^{-1}$, [$SnCl_4$] = $5{\cdot}146 \times 10^{-2}$ mole l.$^{-1}$.
Curve B [LD] = $1{\cdot}774 \times 10^{-1}$ mole l.$^{-1}$, [$SnCl_4$] = $3{\cdot}565 \times 10^{-2}$ mole l.$^{-1}$.
Curve C [LD] = $1{\cdot}07 \times 10^{-1}$ mole l.$^{-1}$, [HCl] = $1{\cdot}039 \times 10^{-1}$ mole l.$^{-1}$.

FIG. 6. *Temperature dependence of* k_c.



The orders of reaction in $SnCl_4$ and HCl have been found to be $1{\cdot}0 \pm 0{\cdot}1$ in each case: there is no optimum [HCl]/[$SnCl_4$] ratio (in agreement with the findings of Part VII [1]) (see Fig. 5). Thus:

$$\text{Rate of formation of cyclic dimer} = k_c\,[\text{LD}][SnCl_4][\text{HCl}]$$

The activation energy, E, for cyclic dimer formation was found to be 8·7 kcal. mole^{-1} by plotting $\log_{10}k_c$ against $1/T$ (Fig. 6).

A check on the extent of the reaction was carried out by taking a known volume of the reacting solution at t_∞ and dissolving it in 98% sulphuric acid. The spectrum of this solution

Table 1. *Conversion of linear dimer into cyclic dimer in the stannic chloride–hydrogen chloride–benzene system.*

k_c (sec.$^{-1}$ mole^{-2} l.^{2})	T	$\Delta H_c^{\ddagger} = (E - RT)$ (kcal. mole^{-1})	$\Delta G_c^{\ddagger}$ (30·0°) (kcal. mole^{-1})	$\Delta S_c^{\ddagger}$ (30·0°) (cal. mole^{-1} deg.$^{-1}$)
$2{\cdot}84 \times 10^{-4}$	30·0°	8·1	22·7	−48·1
$3{\cdot}47 \times 10^{-4}$	40·1			
$7{\cdot}34 \times 10^{-4}$	54·9			

$k_c = k_4k_{2b}/k_{2a} = k_4/K_2$; $\Delta H_c^{\ddagger} = \Delta H_{2b}^{\circ} + \Delta H_4^{\ddagger}$; $\Delta G_c^{\ddagger} = \Delta G_{2b}^{\circ} + \Delta G_4^{\ddagger}$; $\Delta S_c^{\ddagger} = \Delta S_{2b}^{\circ} + \Delta S_4^{\ddagger}$.

was measured. Since the cyclic dimer gives no colour on dissolving in this acid and any residual linear dimer is converted into monomer ion in it, the extent of the reaction can be found from the extinction coefficient of the monomer ion ($\varepsilon_{430} = 2{\cdot}8 \times 10^4$). It was found

XUM

that when no further volume change with time was measurable, the original linear dimer had been completely converted into cyclic dimer to within 0·5%. Thus the formation of cyclic dimer is irreversible, and it does not give any carbonium ions in solution. Thus, as the reaction proceeds the colour of the solution (which becomes intense on adding the hydrogen chloride to the colourless linear dimer–stannic chloride–benzene [1]) gradually fades until it has almost disappeared when no further volume change with time is measurable.

The results are given in Table 1, together with the values of $\Delta G^{\ddagger}$ and $\Delta S^{\ddagger}$.

Discussion

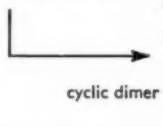
In our previous work we always noted that although two dimers of 1 : 1-diphenylethylene exist, only 1 : 1 : 3 : 3-tetraphenylbut-1-ene was obtained under our conditions. We have now found that the reaction to the cyclic dimer does occur at a measurable rate if the concentration of stannic chloride–hydrogen chloride catalyst is sufficiently great. At concentrations of catalyst which give this measurable rate of formation of cyclic dimer from linear dimer (velocity constant $= 2{\cdot}84 \times 10^{-4}$ sec.$^{-1}$ mole^{-2} l.^{2} at 30·3°, see Table 1), the conversion of monomer into linear dimer occurs extremely rapidly (velocity constant $= 2{\cdot}3 \times 10^{-2}$ mole^{-3} l.^{3} sec.$^{-1}$ at 30·0° [1]). This is why we found no cyclic dimer earlier [1] when the stannic chloride–hydrogen chloride catalyst concentration was that necessary to give a measurable rate for the formation of linear dimer from monomer.

We interpret our results, taken together with those of Part VII,[1] as follows:

$$SnCl_4 + HCl + \underset{\text{monomer}}{CH_2{:}CPh_2} \underset{b}{\overset{a}{\rightleftharpoons}} Me{\cdot}C^+Ph_2\,SnCl_5^- \quad \ldots\ldots\ldots (1)$$

$$Me{\cdot}C^+Ph_2\,SnCl_5^- + CH_2{:}CPh_2 \underset{b}{\overset{a}{\rightleftharpoons}} Me{\cdot}CPh_2{\cdot}CH_2{\cdot}C^+Ph_2\,SnCl_5^- \quad \ldots\ldots\ldots (2)$$

$$Me{\cdot}CPh_2{\cdot}CH_2{\cdot}C^+Ph_2\,SnCl_5^- \underset{b}{\overset{a}{\rightleftharpoons}} \underset{\text{linear dimer}}{Me{\cdot}CPh_2{\cdot}CH{=}CPh_2} + SnCl_4 + HCl \quad \ldots\ldots\ldots (3)$$



(4)

Reactions (1), (2), and (3) are reversible and are discussed in Part VII. The reaction of the 1 : 1 : 3 : 3-tetraphenylbut-1-ene to the indane will go through the 1 : 1 : 3 : 3-tetraphenylbut-1-ene ion, and thus the change will involve reaction (3*b*), followed by irreversible reaction (4).

In the present work we started with the linear dimer. The rate-determining step for the production of monomer from the linear dimer is reaction (2*b*).[4a] In our previous work the catalyst concentration was low, and we followed the conversion of monomer into linear dimer. At high catalyst concentrations, the equilibria (3), (2), and (1) are established rapidly, and it is reaction (4) which becomes the measured rate-determining step.

Thus:

Rate of formation of CD

$$= k_4[LDH^+SnCl_5^-] = (k_4/K_3)[LD][SnCl_4][HCl] = (k_4k_{3b}/k_{3a})[LD][SnCl_4][HCl]$$

This agrees with the relationship we find experimentally:

$$\text{Rate of formation of CD} = k_c[LD][SnCl_4][HCl]$$

and therefore $k_c = k_4/K_3 = k_4k_{3b}/k_{3a}$. Data are given in Tables 1 and 2 and the reaction process is shown diagrammatically in Fig. 7. This diagram shows the reaction of a monomer molecule with another monomer molecule to form a linear dimer, and then the further

TABLE 2. *Conversion of linear dimer into monomer in the stannic chloride–hydrogen chloride–benzene system.**

k_r (sec.$^{-1}$ mole^{-2} l.^{2})	T	$\Delta H_r^{\ddagger} = (E - RT)$ (kcal. mole^{-1})	$\Delta G_r^{\ddagger}$ (30·3°) (kcal. mole^{-1})	$\Delta S_r^{\ddagger}$ (30·3°) (cal. mole^{-1} deg.$^{-1}$)
$1{\cdot}14 \times 10^{-3}$	30·3°	14·4	21·9	−24·8
$2{\cdot}54 \times 10^{-3}$	39·9			
$7{\cdot}82 \times 10^{-3}$	55·0			

* These values are obtained from the results given in Part VII [1] for the conversion of monomer into linear dimer.

$k_r = k_{2b}k_{3b}/k_{3a} = k_{2b}/K_3$; $\Delta H_r^{\ddagger} = \Delta H_{2b}^{\circ} + \Delta H_{2b}^{\ddagger}$; $\Delta G_r^{\ddagger} = \Delta G_{2b}^{\circ} + \Delta G_{2b}^{\ddagger}$; $\Delta S_r^{\ddagger} = \Delta S_{2b}^{\circ} + \Delta S_{2b}^{\ddagger}$.

reaction of the linear dimer, not with another monomer to form a trimer, but with a double bond within its own molecule to form a cyclic dimer.

The process *A* to *B* involves the bringing together of HCl, $SnCl_4$ and two monomer molecules, and so has a very negative entropy change.

The process *D* to *E* involves HCl, $SnCl_4$, and only one olefin molecule, but since it involves a very special orientation of the linear dimer ion to form the cyclic dimer, so it has a very negative entropy change (this orientation can be seen from Courtauld atomic models). The enthalpy change associated with this process is greater than that of step *A* to *B*, presumably because of the greater steric repulsion involved in the cyclisation.

The process *D* to *B* involves HCl, $SnCl_4$, and only one olefin molecule, and so has a much

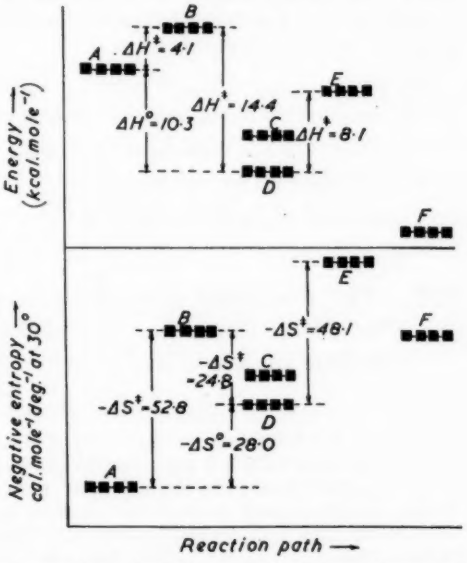


FIG. 7. *Reaction-path diagram.*

A. Initial state of reaction (1); monomer + monomer + HCl + $SnCl_4$.
B. Transition state of reaction (2).
C. Final state of reaction (2); linear dimer ion(+) $SnCl_5$(−).
D. Final state of reaction (3); linear dimer + HCl + $SnCl_4$.
E. Transition state of reaction (4).
F. Final state of reaction (4); cyclic dimer + HCl + $SnCl_4$.

The energy and entropy values are taken from the present paper and from Part VII.[1] The positions of states *C* and *F* are not quantitatively known.

less negative entropy change since the very special orientation of the linear dimer ion described above is not required here. The enthalpy change for this process is large because a single bond is being broken and the second half of a double bond (which is weaker) is being formed.

The linear dimer changes into monomer at a faster rate than it changes into cyclic dimer; k_r/k_o [*i.e.*, $(k_{2b}/K_3)/(k_4/K_3) = k_{2b}/k_4$] varies from 4 at 30° to 10·5 at 55°. This is interesting since the enthalpy of activation for monomer formation is 14·4 kcal. mole^{-1}, compared with a value of 8·1 kcal. mole^{-1} for the formation of cyclic dimer. The rate of the cyclic dimer formation is slower because it is associated with a much more negative entropy of activation (−48·1 cal. mole^{-1} deg.$^{-1}$) than that obtaining for the production of monomer (−24·8 cal. mole^{-1} deg.$^{-1}$).

In the reaction scheme (1), (2), (3), and (4) we have all the steps involved in a cationic polymerisation. Reaction (1*a*) is initiation, (2*a*) is propagation, (3*a*) and (4) are alternative terminations leading to a linear unsaturated molecule or a cyclic saturated molecule. Termination by cyclisation has clearly a very adverse entropy owing to orientation requirements. Thus it will be much more probable that the linear unsaturated molecule is formed from the ion (reaction 3*a*), but since the latter reaction is reversible (3*b*) and reaction (4) is irreversible, the system must all move over to the cyclic saturated molecule in time. At low catalyst concentrations, however, this is a very slow process because equilibrium (3) lies well over to the right. At high catalyst concentrations, however, the concentration of linear dimer ion will be increased [*i.e.*, equilibrium (3) will be moved over to the left] and hence the rate of formation of cyclic saturated molecules will be increased. This means that although the probability of the ion's achieving the right configuration is small, when the number of these ions is increased sufficient find the correct arrangement to give a measurable rate of formation of the cyclic structure.

It has been shown [5] that, in the polymerisation of monomeric α-alkylstyrenes with sulphuric acid, a saturated cyclic and an unsaturated non-cyclic dimer are produced. As the concentration of the catalyst is increased more cyclic dimer is produced relative to unsaturated non-cyclic dimer. This agrees with our results. Hukki [6] also obtained saturated and unsaturated dimers from α*p*-dimethylstyrene using formic acid as dimerising agent. The polymerisation of α-methylstyrene catalysed by stannic chloride in ethyl chloride solution has been studied by Dainton and Tomlinson,[7] who also obtained both saturated and unsaturated polymers.

We thank Messrs. "Shell" Research Ltd. for financial help, and University College, Cardiff, for a British Nylon Spinners Postgraduate Scholarship (to D. P.).

UNIVERSITY COLLEGE, CATHAYS PARK, CARDIFF. [*Received, February 6th*, 1959.]

[5] U.S. Patent 2,329,719, Oct. 28th, 1947.
[6] Hukki, *Acta Chem. Scand.*, 1949, 279—296.
[7] Dainton and Tomlinson, *J.*, 1953, 151.

---

597. *The Formation of Carbonium Ions by the Action of Metal Salts. Part IV.*[1] *Ionisation of Triarylmethyl Chlorides by Friedel–Crafts Catalysts in Acetic Acid.*

By J. L. COTTER and ALWYN G. EVANS.

The ionisation of triarylmethyl chlorides RCl by various Friedel–Crafts catalysts MCl_x has been studied spectrophotometrically in acetic acid. The ionisation leads to the reversible formation of ion pairs $R^+MCl_{x+1}^-$. The ionising power of the metal chlorides decreases along the sequence $SbCl_5 \geqslant FeCl_3 \gg SnCl_4 \gg BiCl_3 > HgCl_2 > SbCl_3$.

EXPERIMENTAL

Materials.—Mercuric chloride. The "AnalaR" reagent was twice sublimed under a high vacuum.

Antimony trichloride. The "AnalaR" reagent was sublimed three times under a high vacuum and portions were collected in sealed capsules.

Stannic chloride. The first sample, prepared by the action of chlorine on tin, was green; the colour was removed by keeping the sample over granulated tin for a few hours. The second sample, prepared by electrolysis of fused stannous chloride, was colourless.[2] A third sample was obtained from Messrs. Hopkin and Williams. The three samples, purified by six distillations under a high vacuum and collected in sealed capsules, gave identical results.

[1] Part III, Bayles, A. G. Evans, and Jones, *J.*, 1957, 1020.
[2] A. G. Evans and Lewis, *J.*, 1957, 2975.

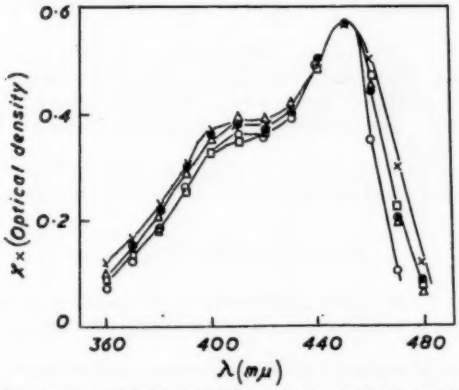
Ferric chloride. B.D.H. anhydrous material was pumped out under a high vacuum and collected in sealed capsules.

Bismuth trichloride. One sample was once sublimed under a high vacuum and a second treated in the same way as ferric chloride; both samples were collected in sealed capsules and gave the same results.

Antimony pentachloride. This was five times distilled under a high vacuum and collected in receivers by means of liquid-air traps; the receivers were then sealed.

Triarylmethyl chlorides. These were prepared from the corresponding carbinols as previously described.[3]

FIG. 1.



△ Antimony trichloride (total concn. $1{\cdot}294 \times 10^{-1}$ mole l.$^{-1}$) and diphenyl-*p*-tolylmethyl chloride (total concn. $3{\cdot}498 \times 10^{-3}$ mole l.$^{-1}$) in acetic acid at 19°; $X = 0{\cdot}780$.
□ Mercuric chloride (total concn. $(6{\cdot}901 \times 10^{-2}$ mole l.$^{-1}$) and diphenyl-*p*-tolylmethyl chloride (total concn. $4{\cdot}574 \times 10^{-3}$ mole l.$^{-1}$) in acetic acid at 20°; $X = 1{\cdot}04$.
× Bismuth trichloride (total concn. $7{\cdot}668 \times 10^{-3}$ mole l.$^{-1}$) and diphenyl-*p*-tolylmethyl chloride (total concn. $1{\cdot}268 \times 10^{-3}$ mole l.$^{-1}$) in acetic acid at 19°; $X = 1{\cdot}34$.
● Stannic chloride (total concn. $5{\cdot}802 \times 10^{-3}$ mole l.$^{-1}$) and diphenyl-*p*-tolylmethyl chloride (total concn. $4{\cdot}636 \times 10^{-4}$ mole l.$^{-1}$) in acetic acid at 20°; $X = 1{\cdot}09$.
○ Diphenyl-*p*-tolylmethyl alcohol (concn. $1{\cdot}238 \times 10^{-5}$ mole l.$^{-1}$) in 98% H_2SO_4; $X = 1$.
X is the factor which has been used to scale the spectra to the same peak height as that of the solution in 98% H_2SO_4.
Curves △ and □ are examples of high MCl_z concentrations (see section on Solvation of Ion Pairs by MCl_z).

Acetic acid. " AnalaR " reagent (f. p. 16·40°) was purified by Eichelberger and La Mer's method.[4] The solvent was refluxed for 14 hr. over triacetyl borate followed by a fractionation. The f. p. of this batch was 16·59° (lit., 16·58° for acetic acid used in conductivity work [4]). All solvent batches were purified by this method and were overlapped as far as possible.

Procedure.—Two master solutions were made up, one containing the organic chloride and the other the metal chloride. Both were of known concentration and so dilute that their light absorption was negligible. Metal chloride solutions were made up as follows. Since mercuric chloride is non-hygroscopic, it was weighed out directly and the solution made up in a graduated flask. For other metal chlorides a small file mark was made near one end of a weighed capsule containing it, which was broken under the solvent. The metal chloride usually dissolved rapidly and the solution was made up in a graduated flask. The capsule pieces were then dried and weighed. Acetic acid solutions of stannic chloride, antimony pentachloride, and ferric chloride so made were too concentrated and were diluted.

The triarylmethyl chloride and metal chloride solutions were then mixed in various ratios. These colourless solutions became intensely yellow on mixing, and their light absorption was measured on a Unicam SP.500 spectrophotometer. Fig. 1 shows typical spectra of the acetic acid solutions containing a triarylmethyl chloride and metal chloride together with the spectrum

[3] A. G. Evans, Jones, and Osborne, *Trans. Faraday Soc.*, 1954, **50**, 167.
[4] Eichelberger and La Mer, *J. Amer. Chem. Soc.*, 1933, **55**, 3633.

of the corresponding alcohol in 98% sulphuric acid. For convenience, these spectra have been scaled up or down to meet the spectrum of the sulphuric acid solution of the alcohol at the absorption maximum. The very close similarity between corresponding spectra for both solvents establishes that the triarylmethyl ion is present in these acetic acid solutions.

The carbonium-ion concentration has been calculated on the assumption that $\int D_\lambda \, d\lambda$ is the same for solutions containing the same concentration of triarylmethyl ions. The alternative method of calculating the ionic concentration, by assuming that $D_{\lambda(\max.)}$ is the same for the same ionic concentration, leads to values which are identical within experimental error with those used.

Molecular-weight Determination.—Cryoscopic measurements were made on the acetic acid solutions of the metal chlorides with a normal Beckmann apparatus, efficient stirring being maintained.

Results

When $[R^+]$ *varies with* $[RCl]^1$ *and with* $[MCl_x]^1$.—The ionisation of diphenyl-*p*-tolylmethyl chloride in the presence of $HgCl_2$, $SbCl_3$, $FeCl_3$, $SnCl_4$, $SbCl_5$, and $BiCl_3$ occurs according to eqn. (1) as seen in Table 1. The values of $K_1 = [R^+MCl_{x+1}^-]/[RCl][MCl_x]$ and of ΔG°_{1a} for this reaction are given in Table 2.

The ionisation of $Ph_3C{\cdot}Cl$ in the presence of $SnCl_4$ and $FeCl_3$ also obeys eqn. (1) as shown by Table 3. The equilibrium constants and the corresponding free-energy changes are given in Table 2.

$$RCl + MCl_x \underset{b}{\overset{a}{\rightleftharpoons}} R^+MCl_{x+1}^- \quad \ldots\ldots\ldots\ldots \quad (1)$$

Equilibrium-constant Units.—The concentrations of reactants used in these Tables are expressed in mole $l.^{-1}$ and g.-ion $l.^{-1}$ units. The free-energy changes have been calculated from

TABLE 1. *Some typical examples of the equilibrium concentrations for mixtures of* RCl *and* MCl_x *in acetic acid where* R *is diphenyl*-p-*tolylmethyl.*

$10^5[MCl_x]$	$10^4[RCl]$	$10^6[R^+MCl_{x+1}^-]$	$\frac{[R^+MCl_{x+1}^-]}{[RCl][MCl_x]}$	$10^5[MCl_x]$	$10^4[RCl]$	$10^6[R^+MCl_{x+1}^-]$	$\frac{[R^+MCl_{x+1}^-]}{[RCl][MCl_x]}$
	$BiCl_3$ at 20°				$SbCl_5$ at 20·5°		
191·7	169·1	2·67	$8{\cdot}27 \times 10^{-2}$	12·13	1·471	8·70	489
383·4	169·1	5·17	$8{\cdot}00 \times 10^{-2}$	18·34	1·442	11·56	423
575·1	169·0	8·26	$8{\cdot}52 \times 10^{-2}$	11·90	2·227	11·00	415
766·8	169·0	11·19	$8{\cdot}73 \times 10^{-2}$	6·17	1·525	3·26	345
958·5	168·9	14·63	$9{\cdot}02 \times 10^{-2}$	12·51	0·730	4·86	532
766·8	422·1	3·34	$10{\cdot}34 \times 10^{-2}$	24·31	1·389	16·90	500
766·8	845·0	5·74	$8{\cdot}88 \times 10^{-2}$	11·74	2·990	12·60	357
766·8	211·3	13·69	$8{\cdot}48 \times 10^{-2}$				
766·8	126·8	8·50	$8{\cdot}71 \times 10^{-2}$		$SnCl_4$ at 20°		
	$FeCl_3$ at 19°			72·7	12·16	5·91	6·67
7·84	3·840	6·58	219	145·3	12·10	12·24	6·97
11·73	3·804	10·20	229	217·9	12·04	18·70	7·14
19·45	3·723	17·93	248	290·5	11·97	24·78	7·12
23·37	3·693	21·30	246	145·8	6·04	7·40	8·45
3·89	3·870	3·56	236	144·5	18·14	19·80	7·58
12·01	2·530	7·43	245	143·9	24·18	26·26	7·55
11·41	5·074	13·42	232	146·1	3·02	3·91	8·92
11·17	6·452	15·76	218		$SbCl_3$ at 21°		
10·85	7·621	18·91	229	428	243·1	1·345	$1{\cdot}29 \times 10^{-2}$
12·32	1·260	4·34	280	1284	243·1	2·717	$0{\cdot}895 \times 10^{-2}$
11·38	5·071	13·70	237	1284	567·2	4·652	$0{\cdot}639 \times 10^{-2}$
	$HgCl_2$ at 19°			2140	405·2	6·174	$0{\cdot}711 \times 10^{-2}$
568	239·2	2·54	$18{\cdot}7 \times 10^{-3}$	2140	324·1	5·282	$0{\cdot}761 \times 10^{-2}$
1136	239·2	5·32	$19{\cdot}5 \times 10^{-3}$	2140	243·1	4·565	$0{\cdot}875 \times 10^{-2}$
1704	239·2	8·04	$19{\cdot}7 \times 10^{-3}$	1712	405·2	5·087	$0{\cdot}735 \times 10^{-2}$
2272	239·2	11·78	$21{\cdot}6 \times 10^{-3}$	1284	405·2	3·891	$0{\cdot}754 \times 10^{-2}$
3408	239·2	18·08	$22{\cdot}1 \times 10^{-3}$	3424	162·0	5·39	$0{\cdot}973 \times 10^{-2}$
2272	59·8	3·54	$26{\cdot}0 \times 10^{-3}$	856	648·2	3·89	$0{\cdot}701 \times 10^{-2}$
2272	119·6	6·21	$22{\cdot}8 \times 10^{-3}$	856	405·2	2·847	$0{\cdot}821 \times 10^{-2}$
2272	179·4	8·90	$21{\cdot}8 \times 10^{-3}$				
2272	358·8	15·82	$19{\cdot}4 \times 10^{-3}$				

XUM

TABLE 2.

RCl	Metal chloride	Mean K_1 * (mole fraction)	Mean $\Delta G_1°$ (kcal. mole^{-1})	Mean temp.
p-$CH_3 \cdot C_6H_4 \cdot CPh_2Cl$	$SbCl_3$	0·145	1·11 ± 0·15	20°
,, ...	$HgCl_2$	0·358	0·59 ± 0·1	18
,, ...	$BiCl_3$	1·57	−0·26 ± 0·1	19
,, ...	$SnCl_4$	106·4	−2·69 ± 0·4	17
,, ...	$FeCl_3$	4,220	−4·81 ± 0·1	18
,, ...	$SbCl_5$	5,655	−4·98 ± 0·2	20
$Ph_3C \cdot Cl$	$SnCl_4$	7·29	−1·14 ± 0·3	18·5
,, ...	$FeCl_3$	353	−3·40 ± 0·1	19·5

* The value of K_1 at 20° can be converted into mole^{-1} l. units by dividing by 17·46.

TABLE 3. *Some typical examples of the equilibrium concentrations for mixtures of* RCl *and* MCl_x *in acetic acid where* R *is triphenylmethyl.*

$10^3[MCl_x]$	$10^4[RCl]$	$10^6[R^+MCl_{x+1}^-]$	$\frac{[R^+MCl_{x+1}^-]}{[RCl][MCl_x]}$	$10^3[MCl_x]$	$10^4[RCl]$	$10^6[R^+MCl_{x+1}^-]$	$\frac{[R^+MCl_{x+1}^-]}{[RCl][MCl_x]}$
	$FeCl_3$ at 19°				$SnCl_4$ at 18°		
0·671	4·500	6·31	20·9	1·436	123·8	10·42	0·584
0·335	4·534	2·92	19·2	2·871	123·7	21·05	0·594
1·002	4·460	10·25	23·0	2·881	61·8	11·23	0·626
1·340	4·437	12·63	21·2	2·887	30·9	5·15	0·574
1·672	4·403	16·05	21·8	0·718	122·8	5·15	0·582
1·009	1·480	4·07	27·5	2·164	123·9	15·52	0·580
1·005	2·971	7·10	23·8	2·877	92·7	16·05	0·595
1·000	5·958	12·63	21·3	4·295	123·6	33·63	0·633
0·997	7·451	15·40	20·7	2·862	185·8	30·26	0·568
				5·737	123·4	47·36	0·675
				2·850	247·4	42·63	0·605

equilibrium constants expressed in mole-fraction units (the recorded values for the density of acetic acid at various temperatures being used).

When $[R^+]$ *varies with* $[RCl]^1$ *but with* $[MCl_x]^n$, *when* $n > 1$.—Mercuric chloride and antimony trichloride are the least effective ionising metal chlorides, and so to produce the same extent of ionisation higher concentrations of these are needed than of the others. When their concentrations are about equal to the concentration of the diphenyl-*p*-tolylmethyl chloride, $[R^+]$ varies with $[RCl]^1$ and with $[MCl_x]^1$ (see Table 1). When, however, the metal chloride is present in large excess $[R^+]$ varies with $[RCl]^1$ but with $[MCl_x]^n$ where $n > 1$. Over this higher concentration range the value of n for $SbCl_3$ is 2·2 ± 0·2 and for $HgCl_2$ is 1·4 ± 0·2 for the interaction of these metal chlorides with diphenyl-*p*-tolylmethyl chloride, and for the interaction of $SbCl_3$ with triphenylmethyl chloride a value of n of up to 3·0 ± 0·2 is found. A typical case is shown in Fig. 2.

Molecular Weights.—Molecular weights are given in Table 4. The freezing-point depressions obtained show that $HgCl_2$, $SbCl_3$, and $BiCl_3$ are monomeric in acetic acid. The depressions obtained for acetic acid solutions of $SnCl_4$, $FeCl_3$, and $SbCl_5$ respectively approximate to those expected for the dimeric species.

TABLE 4. *Molecular weights.*

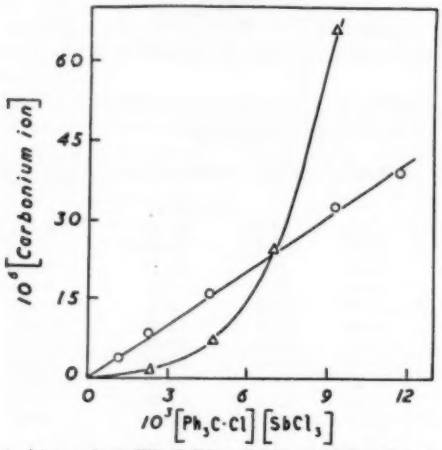
Metal halide	$HgCl_2$	$BiCl_3$	$SbCl_3$	$SbCl_5$	$SnCl_4$	$FeCl_3$
Concn. range (10^{-3} mole l.$^{-1}$) ...	6·2—16	7·1—16·7	21	9·4—32·8	3·2—12·8	1·3—5·3
Mean M (obs.)	272·8	279·1	226·1	638·0	506·0	310·8
M (calc.)	271·6	315·3	228·3	299·3	260·7	162·4

The actual concentrations of the $SnCl_4$, $FeCl_3$, and $SbCl_5$ used in the cryoscopic experiments had to be approximately 10, 100, and 1000 times as great respectively as those required for the ionisation experiments, since the depressions which would be obtained with molar concentrations equal to those used in the ionisation runs would be extremely small. Since the acetic acid solutions of these metal chlorides are so dilute in the spectroscopic work, we have calculated our results on the assumption that at these dilutions the metal chlorides will be monomeric.

Extinction Coefficients of Carbonium Ions.—In Fig. 3 the ionisation is plotted against the total

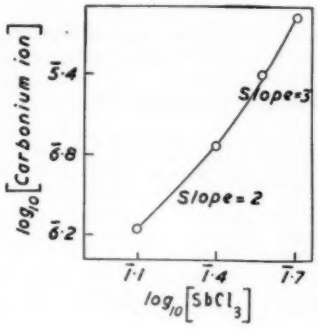
metal chloride concentration. When there is no further change of ionisation the calculated ionisation is between 90 and 100%. This was found in Part II [5] for nitromethane solutions of triphenylmethyl and tri-*p*-tolylmethyl bromides in presence of $HgBr_2$. This establishes that our method of calculating the carbonium-ion concentration, and the values of $\Delta G°$ so obtained, are correct within the experimental accuracy quoted. We have plotted the optical densities

FIG. 2*a*. *Dependence of carbonium-ion concentration on* $[SbCl_3][Ph_3C{\cdot}Cl]$.



△ At constant $[Ph_3C{\cdot}Cl] = 1{\cdot}821 \times 10^{-2}$ mole l.$^{-1}$.
○ At constant $[SbCl_3] = 3{\cdot}831 \times 10^{-1}$ mole l.$^{-1}$.

FIG. 2*b*. *Order in* $SbCl_3$ *at constant* $[Ph_3C{\cdot}Cl]$.



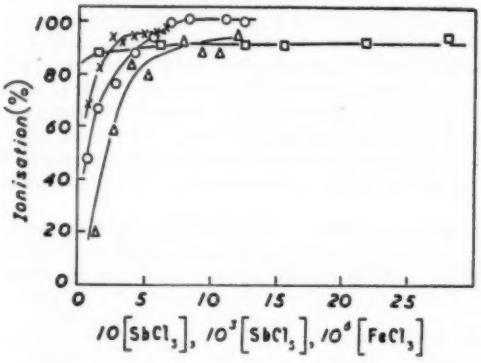


FIG. 3.

× Tri-*p*-tolylmethyl chloride (concn. $5{\cdot}840 \times 10^{-6}$ mole l.$^{-1}$) with ferric chloride.
□ Tri-*p*-tolylmethyl chloride (concn. $9{\cdot}360 \times 10^{-6}$ mole l.$^{-1}$) with antimony pentachloride.
○ Diphenyl-*p*-tolylmethyl chloride (conc. $(1{\cdot}235 \times 10^{-5}$ mole l.$^{-1}$) with antimony pentachloride.
△ Tri-*p*-tolylmethyl chloride (concn. $9{\cdot}360 \times 10^{-6}$ mole l.$^{-1}$) with antimony trichloride.

at maximum ionisation (Fig. 3) against the tri-*p*-tolylmethyl carbonium-ion concentration. This plot gives a straight line passing through the origin, and shows that Beer's law holds accurately for these solutions.

DISCUSSION

Free-energy Changes.—In the absence of metal halide the free energy of ionisation of RCl in acetic acid was 5·8 kcal. mole^{-1} for *p*-$CH_3{\cdot}C_6H_4{\cdot}CPh_2Cl$, and $Ph_3C{\cdot}Cl$ did not give a coloured solution.[6] Table 2 shows that the presence of the metal halide causes a great

[5] Bayles, Cotter, and A. G. Evans, *J.*, 1955, 3104.
[6] A. G. Evans, Price, and Thomas, *Trans. Faraday Soc.*, 1954, **50**, 534.

reduction in the free energy of ionisation. (No change in the heat of ionisation with change in concentration of reagent was observed in these metal halide systems.)

Using the free energy of ionisation as a measure of the ionising efficiency of a metal chloride, we obtain the sequence $SbCl_5 \geqslant FeCl_3 \gg SnCl_4 \gg BiCl_3 > HgCl_2 > SbCl_3$, which we may compare with those obtained for Friedel–Crafts-catalysed reactions. The conversion of pinene into bornyl chloride is accelerated by the presence of Friedel–Crafts catalysts.[7] This is considered to take place by means of a carbonium-ion mechanism and the sequence $SbCl_5 > SnCl_4 > FeCl_3 > HgCl_2 > SbCl_3$ was obtained for the catalyst efficiency, differing from our ΔG° sequence in the interchange of $SnCl_4$ with $FeCl_3$.

The racemisation of 1-phenylethyl chloride takes place in the presence of certain metal chlorides and probably involves a carbonium-ion mechanism.[8] The order of efficiency of the catalysts was $SbCl_5 > SnCl_4 > HgCl_2$, which is the same as our sequence.

An efficiency sequence obtained by Dermer [9] on the basis of yields of *p*-methylacetophenone obtained in the metal chloride-catalysed reaction of acetophenone with methyl chloride is $SbCl_5 > FeCl_3 > SnCl_4 > BiCl_3$, which again agrees with ours.

Jenson and Brown,[10] for the effect of Friedel–Crafts catalysts on the rates of the reaction of benzoyl chloride with toluene and with chlorobenzene, found $SbCl_5 > FeCl_3 \gg SnCl_4 \gg SbCl_3$.

Solvation of Ion Pairs by Metal Halides.—Although under normal conditions the ionisation occurred according to eqn. (1), when very high concentrations of $HgCl_2$ and $SbCl_3$ were used $[R^+]$ varied with $[RCl]^1$ and $[MCl_x]^n$ where $n > 1$. We have seen earlier that in poorly ionising solvents such as benzene and chlorobenzene, the metal chloride also helps to solvate the ion.[1] This effect is also found in the dimerisation of 1 : 1-diphenylethylene by trichloroacetic acid in benzene where the trichloroacetic acid helps to solvate the ions.[11] We attribute the dependence of $[R^+]$ on $[RCl]^1$ and $[MCl_x]^n$ to the fact that the metal halide helps to solvate the ions according to the equation:

$$RCl + nMCl_x \rightleftharpoons (R^+MCl^-_{x+1})_{solv.}$$

where solv. is $(n - 1)MCl_x$ and n is not necessarily an integer since it gives merely a statistical mean of the number of metal chloride molecules associated with an ion.

Ionisation of $Ph_3C{\cdot}Cl$ *in the Presence of* $SnCl_4$ *and* $FeCl_3$.—Ferric chloride is more efficient in promoting ionisation than is stannic chloride. The difference in efficiency as measured by the difference in free energy of ionisation is 2·12 kcal./mole when the organic chloride is diphenyl-*p*-tolylmethyl chloride and 2·26 kcal./mole when the organic chloride is triphenylmethyl chloride (Table 2). Thus the effect on ΔG°_1 of a change in metal halide is the same for different RCl molecules.

The successive introduction of *p*-methyl groups into triphenylmethyl chloride decreases the free energy of ionisation by 1·3 kcal./mole in acetic acid.[5] The corresponding decrease for $FeCl_3$ and $SnCl_4$ in acetic acid solutions is 1·4 and 1·6 kcal./mole respectively (Table 2). Thus the effect on ΔG°_1 of a change of R is the same for different metal halides, and in the absence of metal halides.

Stability of Solutions.—Acetic acid exists completely as the positive ion $(CH_3{\cdot}CO_2H_2^+)$ in concentrated sulphuric acid.[12] The possibility that acetic acid might accept carbonium ions to form the complex $(CH_3CO_2HR^+)$ has been previously considered [5] and it was concluded that if any such ions are formed then their concentration is too small to invalidate the determination of the ionisation equilibrium constants.

In order to detect any interaction between carbonium ions and acetic acid, a 1 cm.

[7] Meerwein and Van Emster, *Ber.*, 1922, **55**, 2500.
[8] Bodendorf and Bohme, *Annalen*, 1935, **516**, 1.
[9] Dermer, *J. Amer. Chem. Soc.*, 1941, **63**, 2881.
[10] Jenson and Brown, *J. Amer. Chem. Soc.*, 1958, **80**, 3039.
[11] A. G. Evans, Jones, and Thomas, *J.*, 1955, 2757.
[12] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, Inc., 1940, p. 46.

glass cell containing an acetic acid solution of stannic chloride and diphenyl-*p*-tolylmethyl chloride was sealed and thermostatted at 55° for three weeks, after which time the optical density at the absorption maximum was unchanged, as it was after 12 months also. This is good evidence that no reaction takes place between the solvent and the carbonium ions in the presence of a Friedel–Crafts catalyst, since it is unlikely that any such reaction would be instantaneous.

One of us (J. L. C.) thanks D.S.I.R. for a Maintenance Allowance. We thank the Chemical Society for a grant from their Research Fund.

UNIVERSITY COLLEGE, CARDIFF. [*Received, March 13th*, 1959.]

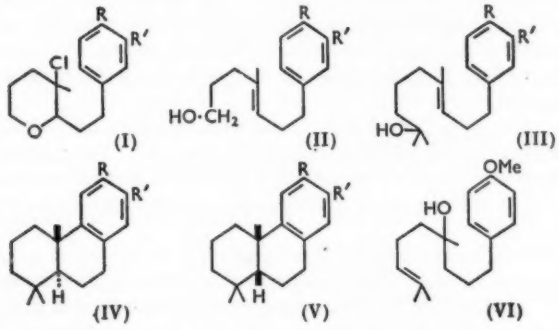
---

598. *Reduced Cyclic Compounds. Part VIII.* The Synthesis of (±)-6-Methoxypodocarpa-5,7,13(14)-triene and (±)-Abieta-5,7,13(14)-triene.†*

By M. F. ANSELL and B. GADSBY.

The action of polyphosphoric acid on 9-*m*-isopropylphenyl- and 9-*p*-methoxyphenyl-2,6-dimethylnon-*trans*-6-en-2-ol, whose preparations are described, is shown to yield respectively mixtures of (±)-11α- and -11β-abieta-5,7,13(14)-triene, and (±)-6-methoxy-11α- and -11β-podocarpa-5,7,13(14)-triene. The latter mixture has been separated.

THE availability of 5,6-dihydro-3-methyl-4*H*-pyran [1] enables Ansell and Selleck's synthesis [2] of 1,2,3,4,9,10,11,12-octahydrophenanthrenes to be extended to the 12-methyl derivatives. To this end 9-*m*-isopropylphenyl- (III; R = H, R′ = Pr^i) and 9-*p*-methoxyphenyl-2,6-dimethylnon-*trans*-6-en-2-ol (III; R = OMe, R′ = H) were prepared. These nuclear substituents were chosen so that the cyclisation products would be the known abieta-5,7,13(14)-triene (IV; R = H, R′ = Pr^i) and 6-methoxypodocarpa-5,7,13(14)-triene (IV; R = MeO, R′ = H) or stereoisomeric with them.



The alcohols (III) were prepared as follows: the Grignard reagents of the appropriately substituted phenethyl chloride were coupled with 2,3-dichlorotetrahydro-3-methylpyran to yield the compounds (I) which on ring scission with sodium gave the alcohols (II). These were converted into the required tertiary alcohols (III) by treatment of the Grignard

* Part VII, *J.*, 1959, 329. † The nomenclature used is that of Klyne, *J.*, 1953, 3072.

[1] Ansell and Gadsby, *J.*, 1958, 3388.
[2] Ansell and Selleck, *J.*, 1956, 1238.

reagent of the derived chloride (prepared *via* the toluene-*p*-sulphonate) with acetone. The alcohols prepared in this way are considered to have a *trans*-configuration (cf. ref. 1).

Treatment of the methoxy-alcohol (III; R = OMe, R′ = H) with polyphosphoric acid yielded a mixture of (±)-6-methoxy-11α- and -11β-podocarpa-5,7,13(14)-triene, as shown by analysis and dehydrogenation to 6-methoxy-1-methylphenanthrene. The pure crystalline (±)-11β-isomer (V; R = MeO, R′ = H) was obtained from this mixture and was identical with that obtained by Fétizon and Delobelle [3] (following the work of Nasipuri [4]) by cyclisation of the alcohol (VI) with polyphosphoric acid. After removal of the (±)-11β-isomer the residual liquid product had an infrared spectrum which differed from that of the (±)-11β-isomer but was essentially the same as that of the 11α-isomer, which is considered to be the major component of the liquid fraction.

The *m*-isopropyl alcohol (III; R = H, R′ = Pr^i) with polyphosphoric acid yielded an essentially (97·8%) saturated product, which with 2,4-dinitrobenzenesulphenyl chloride gave, after chromatography, a product containing not more than 1·5% of diolefinic material. The infrared spectrum revealed no absorption at 750—810 cm.$^{-1}$ (characteristic of 1,2,3-aromatic trisubstitution) but absorption at 820 and 876 cm.$^{-1}$ attributable to a 1,2,4-trisubstituted benzene ring and at 1361, 1370, and 1380 cm.$^{-1}$ indicating the presence of a methyl and *gem*-dimethyl group.[5] These results are consistent with the product's being a mixture of (±)-11α- and -11β-abieta-5,7,13(14)-triene (IV and V; R = H, R′ = Pr^i). This conclusion was confirmed by comparison of the infrared spectrum of the cyclisation product with that of authentic abieta-5,7,13(14)-triene.[6]

Conversion of 6-methoxypodocarpa-5,7,13(14)-triene-16-oic acid (6-methoxypodocarpic acid) and abieta-5,7,13(14)-trien-15-oic acid (dehydroabietic acid) into the parent hydrocarbons has been [6,7] effected by Rosenmund reduction of the acid chloride followed by Kishner–Wolff reduction of the aldehyde. An attempt was made to employ an alternative procedure, namely, reduction of the acid to the alcohol followed by reduction of the derived toluene-*p*-sulphonate with lithium aluminium hydride, which has been successful [8] in the 9-methyldecalin series. Although the toluene-*p*-sulphonates were readily obtained the final reduction was not satisfactory. In the methoxy-series the product could not be obtained free from sulphur, and in the isopropyl series a saturated hydrocarbon product was obtained whose properties were not those of abieta-5,7,13(14)-triene. If the final reduction occurs through an S_Ni mechanism,[9] then a neopentyl-type rearrangement is possible to yield 1-ethyl-1,2,3,4,9,10,11,12-octahydro-7-isopropylphenanthrene. Our results are consistent with the product's being a mixture of the latter and abieta-5,7,13(14)-triene.

Experimental

4-Methoxy- and 3-Isopropyl-phenethyl Chloride.—Thionyl chloride (130 g.) was added slowly to a stirred, boiling solution of the substituted phenethyl alcohol (4-methoxy,[10] 3-isopropyl [11]) (0·9 mole) in benzene (150 ml.). The solution was boiled and stirred until evolution of hydrogen chloride ceased, then cooled, and washed successively with 50 ml. portions of 10% aqueous sodium chloride, and distilled. In this way were prepared 4-methoxyphenethyl chloride (144 g., 91%), b. p. 136—139°/24 mm., n_D^{20} 1·5372 (lit.,[10] b. p. 129·5—131°/10 mm.) and *3-isopropylphenethyl chloride* (140 g., 85%), b. p. 120°/11 mm., n_D^{20} 1·5165 (Found: C, 72·1; H, 8·3; Cl, 19·8. $C_{11}H_{15}Cl$ requires C, 72·4; H, 8·2; Cl, 19·5%).

3-Chlorotetrahydro-3-methyl-2-phenethylpyran Derivatives.—A solution of 2,3-dichlorotetrahydro-3-methylpyran [1] [from 5,6-dihydro-3-methyl-4*H*-pyran (40 g., 0·41 mole)] in ether

[3] Fétizon and Delobelle, *Compt. rend.*, 1958, **246**, 2774.
[4] Nasipuri, *Chem. and Ind.*, 1957, 425.
[5] Bellamy, "Infra-red Spectra of Complex Molecules," Methuen, London, 1954.
[6] Jeger, Durst, and Buchi, *Helv. Chim. Acta*, 1947, **30**, 1853.
[7] Campbell and Todd, *J. Amer. Chem. Soc.*, 1942, **64**, 928.
[8] Hussey, Liao, and Baker, *ibid.*, 1953, **75**, 4727; Dauben, Tweit, and MacLean, *ibid.*, 1955, **77**, 48.
[9] Cf. Corey, Howell, Boston, and Young, and Sneen, *ibid.*, 1956, **78**, 5036.
[10] Plimmer, Short, and Hill, *J.*, 1938, 694.
[11] Haworth and Barker, *J.*, 1939, 1299.

(100 ml.) was added dropwise to a stirred solution of the Grignard reagent prepared from the substituted phenethyl chloride (0·55 mole) and magnesium (13·4 g.) at such a rate that gentle refluxing was maintained. The stirred mixture was boiled for 1 hr., then poured on ice and ammonium chloride. The aqueous layer was extracted with ether, and the dried (K_2CO_3) combined ethereal solutions were distilled. In this way were prepared: 3-*chlorotetrahydro*-2-4′-*methoxyphenethyl*-3-*methylpyran* (64·5 g., 59%), b. p. 148—152°/0·1 mm., n_D^{17} 1·5300 (Found: C, 67·5; H, 7·85; Cl, 12·8. $C_{15}H_{21}O_2Cl$ requires C, 67·1; H, 7·8; Cl, 13·2%) [1,4-bis-*p*-methoxyphenylbutane, b. p. 177—182°/0·5 mm., m. p. 75—77° (Found: C, 80·0; H, 8·15. Calc. for $C_{18}H_{22}O_2$: C, 79·8; H, 8·15%), was also obtained (lit.,[12] m. p. 78—79°)], and 3-*chlorotetrahydro*-2-3-*isopropylphenethyl*-3-*methylpyran* (61·4 g., 53·5%) b. p. 126—127°/0·01 mm., n_D^{20} 1·5170 (Found: C, 71·8; H, 8·75; Cl, 13·3. $C_{17}H_{25}OCl$ requires C, 71·1; H, 9·25; Cl, 13·1%).

7-p-*Methoxyphenyl*-4-*methyl*- *and* 7-m-*Isopropylphenyl*-4-*methyl*-*hept*-trans-4-*en*-1-*ol*.—A solution of one of the above 3-chlorotetrahydropyrans (0·24 mole) in ether (100 ml.) was added to a stirred suspension of sodium sand (12 g.) in ether (50 ml.) at such a rate that steady refluxing of the solvent was maintained, and the mixture then stirred for a further hour. Water was then added (caution) to yield two phases, which were separated, and the aqueous phase was extracted with ether. The dried ($MgSO_4$) combined extracts were distilled. In this way were prepared: 7-p-*methoxyphenyl*-4-*methylhept*-trans-4-*en*-1-*ol* (46 g., 81%), b. p. 160—164°/0·1 mm., n_D^{20} 1·5286 (Found: C, 77·2; H, 9·4. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%), and 7-m-*isopropylphenyl*-4-*methylhept*-trans-4-*en*-1-*ol* (46 g., 78%), b. p. 135°/0·02 mm., n_D^{20} 1·5168 (Found: C, 83·1; H, 10·5. $C_{17}H_{26}O$ requires C, 83·0; H, 10·6%).

7-*Chloro*-4-*methyl*-1-*phenylhept*-trans-3-*ene Derivatives*.—One of the above alcohols (0·25 mole) was added slowly to a stirred slurry of toluene-*p*-sulphonyl chloride (57 g.) in " AnalaR " pyridine (30 g.) at 20° ± 2°. After being left overnight the mixture was diluted with water and extracted with ether. The extract was washed with 50 ml. portions of 25% sulphuric acid, water, saturated aqueous sodium hydrogen carbonate, and water. Evaporation of the dried ($MgSO_4$) extract gave the crude toluene-*p*-sulphonate (*ca.* 80%) as a viscous oil. The latter was added to a warm (50°) solution of anhydrous lithium chloride in 2-ethoxyethanol (100 ml.), the resulting mixture stirred at 110° for 4 hr., and the solvent then removed under reduced pressure. Water was added to the residue which was extracted with ether (2 × 100 ml.), and the dried ($MgSO_4$) extract was distilled (from K_2CO_3). In this way were prepared: 7-*chloro*-1-p-*methoxyphenyl*-4-*methylhept*-trans-3-*ene* (40 g., 80%) b. p. 143—148°/0·2 mm., n_D^{20} 15248 (Found: C, 71·1; H, 8·2; Cl, 13·9. $C_{15}H_{21}OCl$ requires C, 71·3; H, 8·3; Cl, 14·05%), and 7-*chloro*-1-m-*isopropylphenyl*-4-*methylhept*-trans-3-*ene* (48 g., 72%), b. p. 178—181°/7 mm., n_D^{20} 1·5144 (Found: C, 77·0; H, 9·3; Cl, 13·35. $C_{17}H_{25}Cl$ requires C, 77·1; H, 9·5; Cl, 13·4%).

2,6-*Dimethyl*-9-*phenylnon*-trans-6-*en*-2-*ol Derivatives*.—Dry acetone (10 g.) was added to a stirred solution of the Grignard reagent derived from one of the above chlorides (0·087 mole) and magnesium (0·22 g.) in ether (40 ml.) at such a rate that steady refluxing was maintained. The mixture was stirred and boiled for 15 min., then left overnight. Excess of 10% sulphuric acid was added, the ethereal layer separated, the aqueous layer extracted with ether, and the dried (K_2CO_3) combined extracts were distilled. In this way were prepared: 9-p-*methoxyphenyl*-2,6-*dimethylnon*-trans-6-*en*-2-*ol* (12 g., 50%), b. p. 135—138°/0·01 mm., n_D^{20} 1·5161 (Found: C, 77·8; H, 9·9. $C_{18}H_{22}O_2$ requires C, 78·3; H, 10·1%), and 9-m-*isopropylphenyl*-2,6-*dimethylnon*-trans-6-*en*-2-*ol* (15·5 g., 62%), b. p. 157—159°/0·1 mm., n_D^{20} 1·5073 (Found: C, 82·9; H, 11·1. $C_{20}H_{32}O$ requires C, 83·3; H, 11·1%).

Cyclisation of 9-p-*Methoxyphenyl*-2,6-*dimethylnon*-trans-6-*en*-2-*ol*.—This alcohol (5 g.) was added to stirred warm (40°) polyphosphoric acid (50 g.), and the mixture vigorously stirred at 80° for 45 min., then cooled, poured on ice, and extracted with ether (2 × 100 ml.); the extract was dried ($MgSO_4$) and distilled, to give 1,2,3,4,9,10,11,12-octahydro-6-methoxy-1,1,12-trimethylphenanthrene (4·2 g., 90%), b. p. 130—136°/0·1 mm. Microhydrogenation indicated 1·1% of diolefinic material and dehydrogenation with selenium, at 300—350° for 50 hr., gave 6-methoxy-1-methylphenanthrene, isolated as the picrate, m. p. 139—141° (lit.,[13] m. p. 140—141·5°). The product was eluted from a column of alumina with pentane, and on removal of the solvent the residue slowly deposited (±)-6-methoxy-11β-podacarpa-5,7,13(14)-triene (0·36 g.) as prisms, m. p. and mixed m. p. with an authentic [3] sample 50—51·5° (Found: C, 84·0; H, 9·9. Calc. for $C_{18}H_{26}O$: C, 83·7; H, 10·1%). A further quantity (0·5 g.; m. p. 50—51·5°) of

[12] Haworth and Moore, *J.*, 1946, 633.
[13] Sherwood and Short, *J.*, 1938, 1006.

this compound was obtained by cooling a pentane solution of the mother-liquors to −60°. The liquid portion of the product, n_D^{20} 1·5489 (Found: C, 83·3; H, 9·6%), was accepted as (±)-6-methoxy-11α-podocarpane (Raman and Rao [14] record b. p. 145—147°/0·8 mm., n_D^{26} 1·5465; Fétizon and Delobelle [3] record b. p. 120—123°/5 × 10^{-3} mm., n_D^{19} 1·5447).

Cyclisation of 9-m-*Isopropylphenyl*-2,6-*dimethylnon*-trans-6-*en*-2-*ol*.—This alcohol (15 g.) was treated with polyphosphoric acid (150 g.) at 80—100° for 45 min., the subsequent procedure being as for the methoxy-analogue. Distillation gave a mixture of predominantly 11α- and 11β-abieta-5,7,13(14)-triene (10·5 g., 75%), b. p. 130—141°/0·1 mm., n_D^{20} 1·5336—1·5364 (microhydrogenation showed 2·2% of diolefinic material). This material, together with 2,4-dinitrobenzenesulphenyl chloride (0·375 g.) in glacial acetic acid (20 ml.), was heated on a steam-bath for 15 min., then cooled and poured into water. The mixture was continuously ether extracted overnight. The extract was washed with 10% aqueous sodium carbonate, dried ($MgSO_4$), and evaporated, and the residue was eluted from a column of alumina, with pentane, to yield 7·3 g. of material (microhydrogenation showed 1·5% of diolefinic material). Fractional distillation (micro-spinning band column, E. Haage, Mulheim) gave material of b. p. 186·5—189°/14 mm., n_D^{20} 1·5360—1·5369 (Found: C, 88·2; H, 11·4. Calc. for $C_{20}H_{30}$: C, 88·9; H, 11·1%) (lit.,[15] for 1,2,3,4,9,10,11,12-octahydro-7-isopropyl-1,1,12-trimethylphenanthrene, b. p. 107—114°/0·1 mm., n_D^{20} 1·5270).

Toluene-p-*sulphonates of* 6-*Methoxypodocarpa*-5,7,13(14)-*trien*-16-*ol and Abieta*-5,7,13(14)-*trien*-15-*ol*.—The appropriate alcohol (0·015 mole) [obtained by reduction (for 18 hr.) of the corresponding acids with lithium aluminium hydride in boiling di-n-butyl ether [16]] was treated in pyridine (40 ml.) with toluene-*p*-sulphonyl chloride (3·05 g., 0·016 mole) in pyridine (20 ml.) and boiled for 12 hr., then cooled and poured into water (150 ml.). The mixture was made alkaline with 2N-ammonia and extracted with ether (2 × 50 ml.). The residue obtained on evaporation of the dried ($MgSO_4$) ether extract was crystallised from ether–pentane and then ethanol. In this way were prepared the *toluene*-p-*sulphonate* (2·25 g., 35%), m. p. 81—82°, of 6-methoxypodocarpa-5,7,13(14)-trien-16-ol (Found: C, 70·0; H, 7·7. $C_{35}H_{32}O_4S$ requires C, 70·1; H, 7·5%), and the *toluene*-p-*sulphonate* (3·04 g., 46%), m. p. 86°, of abieta-5,7,13(14)-trien-15-ol (Found: C, 73·35; H, 8·3. $C_{27}H_{36}O_3S$ requires C, 73·6; H, 8·3%).

Reduction of toluene-p-*sulphonates*. A solution of abieta-5,7,13(14)-trien-15-yl toluene-*p*-sulphonate (24 mmoles) in di-n-butyl ether (50 ml.) was added to a suspension of lithium aluminium hydride (2·3 g., 60 mmoles) in dibutyl ether (50 ml.), and the mixture boiled for 5 hr. Water and 2N-hydrochloric acid were added to the cool mixture, which was then continuously extracted with ether for 14 hr. The residue obtained on evaporation of the dried ($MgSO_4$) extracts was dissolved in pentane and passed through a column of alumina, and the eluant was distilled. The product (3·0 g., 44%), b. p. 154—156°/0·1 mm., n_D^{20} 1·5452, $[\alpha]_D$ +128° in chloroform (Found: C, 88·9; H, 10·8. Calc. for $C_{20}H_{30}$: C, 88·8; H, 11·1%), was saturated to hydrogen in the presence of Adams catalyst and did not form a crystalline dinitro-derivative. Jeger *et al.*[6] record for abieta-5,7,13(14)-triene b. p. 135°/0·05 mm., $[\alpha]_D$ +5° (dinitro-derivative, m. p. 187—188°). Dupont [17] records m. p. 46° for 1-ethyl-1,2,3,4,9,10,11,12-octahydro-7-isopropyl-phenanthrene.

The reduction product of 6-methoxypodocarpa-5,7,13(14)-trien-16-yl toluene-*p*-sulphonate was insoluble in pentane and could not be purified.

The authors are indebted to the D.S.I.R. for an award (to B. G.), to the University of London Central Research Fund for financial assistance, to the Hercules Powder Company for a gift of dehydroabietonitrile, to Dr. F. J. T. Grigg (D.S.I.R., New Zealand) for a gift of podocarpic acid, to Dr. S. S. Brown for a gift of *m*-bromocumene, and to Professor Fétizon for copies of the infrared spectra of (±)-6-methoxy-11α- and -11β-podocarpa-5,7,13(14)-triene and a sample of the 11β-isomer.

QUEEN MARY COLLEGE, UNIVERSITY OF LONDON,
MILE END ROAD, LONDON, E.1. [*Received, March 24th*, 1959.]

[14] Rao and Raman, *Tetrahedron*, 1958, **4**, 294.
[15] Caliezi and Schinz, *Helv. Chim. Acta*, 1952, **35**, 1649.
[16] Cf. Zeiss, Slimowicz, and Pasternak, *J. Amer. Chem. Soc.*, 1948, **70**, 1981.
[17] Dupont, *Bull. Soc. chim. France*, 1958, **25**, 17.

XUM

599. *Bromamines. Part I. Mono- and Di-bromamine.*

By J. K. Johannesson.

Bromine reacts with ammonium salts in aqueous solution at neutral pH to form both mono- and di-bromamine which have characteristic ultraviolet absorption spectra. The bromamines differ from their chlorine analogues in that they are strong oxidizing agents at neutral pH; in the case of monobromamine this is probably due to the presence of the monobromammonium ion at these pH values.

The *N*-bromo-alkylamines have been known for a long time and in some instances have been characterised as crystalline compounds.[1] That ammonia itself reacts with bromine has also been known and has been used to determine ammonia by addition of an excess of sodium hypobromite ($3BrO^- + 2NH_3 \longrightarrow N_2 + 3Br^- + 3H_2O$) and back-titration with thiosulphate after addition of iodide,[2] or, more recently, by amperometric titration with hypobromite [3] or with hypochlorite in the presence of bromide.[4] The estimation has also been performed coulometrically with electrolytically generated hypobromite.[5]

Bromamine itself was first studied by Moldenhauer and Burger [6] who showed that it was formed by the action of bromine on ammonia in ether, and that amongst other reactions it oxidized potassium iodide to iodine. Johannesson [7] has shown that in neutral solutions monobromamine is stable in the presence of a large excess of ammonium salts and that it has a characteristic ultraviolet spectrum.

With lower ammonia : bromine ratios some dibromamine is formed, as reported by the author [8] and by Coleman, Yager, and Soroos.[9] It could be expected that reaction of bromine with ammonia would be similar to that of chlorine, where monochloramine, dichloramine, and nitrogen trichloride are formed. These chlorine compounds have been studied spectrophotometrically by Metcalf,[10] by Corbett, Metcalf, and Soper,[11] and by Weil and Morris.[12] Metcalf [10] showed that *N*-monochloro-amines had maxima at 260—240 mμ, monochloramine at 240, dichloramine at 297, and nitrogen trichloride at 340 mμ. The present author [7] found monobromamine to have a maximum at 277 mμ, and dibromamine at <230 mμ, but found no evidence for the existence of nitrogen tribromide in aqueous solution. The present paper presents data on the conditions of formation, and on the existence of the monobromammonium ion and dibromamine, together with their polarographic and chemical properties. A comparison is made with the corresponding chlorine compounds.

Monobromamine.—In aqueous solution, bromine undergoes the reaction, $Br_2 + H_2O \longrightarrow H^+ + Br^- + HOBr$, with formation also of perbromides Br_3^- and Br_5^-. As the reaction of bromine with ammonia or ammonium salts may be expected to proceed by the action of hypobromous acid on the ammonium ion $HOBr + NH_4^+ \longrightarrow NH_2Br + H_2O + H^+$ this reaction would be favoured by conditions giving the greatest concentrations of hypobromous acid. Low pH and/or the presence of bromide ions will reduce the amount of hypobromous acid, and so should retard the action of bromine on ammonia. In agreement, no reaction occurred at pH 4 in the presence of an excess of bromide.

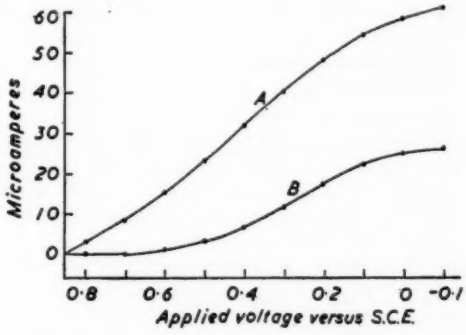
[1] Hofmann, *Ber.*, 1883, **16**, 558; Norris, *Amer. Chem. J.*, 1898, **20**, 51; Willstätter and Hottenroth, *Ber.*, 1904, **37**, 1775.
[2] Kolthoff and Laur, *Z. analyt. Chem.*, 1928, **73**, 177.
[3] Kolthoff, Stricks, and Morren, *Analyst*, 1953, **78**, 405.
[4] Laitinen and Woerner, *Analyt. Chem.*, 1955, **27**, 215.
[5] Arcand and Smith, *ibid.*, 1956, **28**, 440.
[6] Moldenhauer and Burger, *Ber.*, 1929, **62**, 1615.
[7] Johannesson, *New Zealand J. Sci. Technol.*, 1955, *B*, **36**, 600.
[8] *Idem, Chem. and Ind.*, 1958, 97.
[9] Coleman, Yager, and Soroos, *J. Amer. Chem. Soc.*, 1934, **56**, 965.
[10] Metcalf, *J.*, 1942, 148.
[11] Corbett, Metcalf, and Soper, *J.*, 1953, 1927.
[12] Weil and Morris, *J. Amer. Chem. Soc.*, 1949, **71**, 3123.

XUM

At this pH, in the absence of added bromide, the reaction commenced but was rapidly halted through the conversion of the available bromine into the unreactive tribromide ion, the bromide ion for this reaction arising from rapid decomposition of the products at this pH. Attempts to use bromide-free hypobromous acid were also unsuccessful, for the same reasons. The formation of the tribromide ion was followed spectrophotometrically, as this ion has a very intense absorption near 260 mμ. The unreactivity of the tribromide ion towards aromatic compounds has been noted by other workers.[13]

At neutral pH, bromine reacted readily with ammonium salts even in the presence of an excess of bromide ion, giving monobromamine in the presence of an excess of ammonium ion. At pH 8·2, monobromamine had an absorption maximum at 277 mμ, and a molar absorbance of 260. At slightly lower pH values, and in the presence of an excess of ammonium ion to suppress the reaction, $H^+ + 2NH_2Br \longrightarrow NHBr_2 + NH_4^+$, the reaction $H^+ + NH_2Br \longrightarrow NH_3Br^+$, occurred. Presence of the monobromammonium ion NH_3Br^+ was shown by the absorption spectra, which with decreasing pH values showed a decrease in absorbance at 277 mμ, and an increase in the region below 230 mμ. Over the pH range concerned, a family of absorption curves was obtained with well-defined isosbestic points at 260 and 310 mμ.

The positive ionic nature of the substance formed in the above reaction was demonstrated by electrodialysis, active bromine passing to the cathodic chamber where it was combined with fluorescein to form eosin, after the manner of the positive bromine-ion experiments of Gonda-Hunwald, Graf, and Korosy.[14]



Current–voltage curves for hypobromite (A) and monobromamine (B) with the platinum electrode versus *the S.C.E.*

Attempts to determine the molar absorbance of the monobromammonium ion by lowering the pH to the point where only the ion would be present were unsuccessful owing to the rapidity of decomposition and the presence of hydrolysis at these lower pH values.

By Weil and Morris's method,[12] measurement of the change of absorbance with change of pH gave for the equilibrium constant $K_a = [H^+][NH_2Br]/[NH_3Br^+]$ the average value of $1{\cdot}07 \times 10^{-6}$ (see Table). Correcting for activity effects gives the true thermodynamic constant $K_a = 0{\cdot}408 \times 10^{-6}$. Since $K_b = K_w/K_a$, $K_b = 2 \times 10^{-8}$, to be compared with $1{\cdot}8 \times 10^{-5}$ for ammonia and 1×10^{-15} estimated by Weil and Morris [12] for monochloramine. The weaker basicity of the monochloramine and monobromamine may be ascribed to the greater inductive effects of the halogens.

Dibromamine.—At pH 8·3, a low ratio ammonium : bromine gave a different spectrum with high absorbance in the region below 230 mμ, and a reduced absorbance near 277 mμ due to the formation of dibromamine. This work has been described elsewhere by the author.[8] Successive additions of ammonium sulphate solution to a solution prepared as above caused the spectrum to change progressively to that of pure monobromamine as

[13] Bradfield, Davies, and Long, *J.*, 1949, 1393; Bartlett and Tarbell, *J. Amer. Chem. Soc.*, 1936, **58**, 467.

[14] Gonda-Hunwald, Graf, and Korosy, *Nature*, 1950, **166**, 68.

Acid dissociation constant of monobromammonium ion. Molar absorbance for monobromamine base is 260.

$10^6[H^+]$	$\varepsilon_{obs.}$	$\varepsilon_B - \varepsilon_{obs.}$	$10^{-6}(\varepsilon_B - \varepsilon_{obs.})/[H^+]$	10^6K_a	$10^6[H^+]$	$\varepsilon_{obs.}$	$\varepsilon_B - \varepsilon_{obs.}$	$10^{-6}(\varepsilon_B - \varepsilon_{obs.})/[H^+]$	10^6K_a
2·56	165	95	37·1	1·08	0·850	200	60	70·8	1·08
1·91	174	86	45·0	1·08	0·605	210	50	82·7	1·04
1·44	182	78	54·1	1·06	0·480	218	42	88·0	1·09
1·12	190	70	62·5	1·04					
								Average	1·07

represented by $NHBr_2 + NH_4^+ \longrightarrow 2NH_2Br + H^+$. It was not possible to determine the equilibrium constant for this reaction. These solutions were very unstable and it appears that there was a minimum ratio for any stability for a mixture of the mono- and di-bromamines, below which there is almost instantaneous decomposition. Attempts at electrodialysis were not successful owing to the speedy decomposition, and the minimum ratio described in the preceding sentence.

Polarographic Behaviour.—With an electrode system consisting of a rotating platinum electrode together with a saturated calomel half-cell (S.C.E.) free halogens give diffusion currents which commence near +0·8 v *versus* the S.C.E.[3] The wave commences near +0·1 v *versus* the S.C.E. for monochloramine and at even more negative values for dichloramine. The exact values are a function of the pH and the pre-treatment of the electrodes. For monobromamine the diffusion current was found to commence near +0·5 v *versus* the S.C.E. and for solutions containing dibromamine the wave commenced near that for free bromine. In each case, however, the current was much lower than that for free bromine at the same applied E.M.F. Addition of ammonium salts to a solution containing dibromamine gave diffusion currents intermediate in value until, with an excess of ammonium ion present, the wave was that of monobromamine.

Chemical Reactions.—Both monobromamine and dibromamine act as strong oxidizing agents and, in neutral solution, oxidize phenyl arsenoxide, sodium arsenite, Methyl Orange, Methyl Red, benzidine, *o*-tolidine, and potassium iodide amongst other compounds. By contrast, monochloramine liberates iodine from iodide in neutral solutions but does not oxidize the other compounds unless the pH is 3 or less. Dichloramine is less reactive and does not oxidize even iodide unless the solutions are acidified to pH 4 or less. In solution at pH 8 monobromamine reacts with dimethylamine to form *N*-bromodimethylamine, probably by the reaction, $NH_3Br^+ + Me_2NH \longrightarrow Me_2NHBr^+ + NH_3$, an equilibrium mixture being formed. This reaction was observed spectrophotometrically and will be discussed in a further communication.

Discussion.—It has been shown that both monobromamine and dibromamine may be formed by the action of bromine on ammonia solutions at neutral pH and exhibit characteristic ultraviolet absorption spectra. In more acid solutions the monobromammonium ion is formed with K_b of 2×10^{-8}.

The stronger oxidizing properties of monobromamine than of monochloramine are probably due to the presence of significant amounts of the monobromammonium ion. Thus at pH 7·0 approximately 10% is present as the ion, and at pH 8·0 approximately 1%, the actual amount depending upon the ionic strength of the solution and the temperature. Monochloramine with K_b 10^{-15} will have only about one part in 10^8, at pH 7, of the positive ion, an insignificant amount. The oxidizing reactions of these compounds probably proceed: $NH_3Br^+ \longrightarrow NH_3 + Br^+$. Brown and Soper [15] demonstrated that chlorination of phenol by *N*-chlorodialkylamine involved the action of the *N*-chlorodialkylammonium ion on phenol. Monobromamine and dimethylamine probably react by a similar mechanism, whilst monochloramine does not react with dimethylamine under these conditions. Dichloramine is a much weaker oxidizing agent than monochloramine, but

[15] Brown and Soper, *J.*, 1953, 3576.

by contrast dibromamine appears to be a stronger agent than monobromamine, as shown by its polarographic behaviour.

In the ultraviolet spectrum, the bromamines differ from the chloramines in that the dibromamine has an absorption maximum at a much lower wavelength than monobromamine whereas dichloramine has an absorption maximum (297 mμ) at a greater wavelength than monochloramine has (240 mμ), as demonstrated by Metcalf.[10]

Experimental

Ultraviolet absorption spectra were measured with an Unicam S.P. 500 spectrophotometer, and the pH measurements with a Beckman Model G pH meter.

For electrodialysis a multicompartment apparatus was used. In the absence of the extra electrode compartment, bromide ion would migrate to the anode and there be oxidized to bromine, which would react with the fluorescein and form eosin, giving erroneous results. With monobromamine in the presence of a large excess of ammonium salt at pH 8·2 in the central compartment and with 100 v applied the quantities of eosin formed in the reaction compartments were small and equal, being due in each case to diffusion. With the conditions as above, but at pH 6·0, the fluorescein in the cathodic compartment was rapidly converted into eosin, showing the presence of a stable positive ion containing active bromine.

Conventional forms of rotating platinum electrode systems were used for polarography; for measurements at negative applied potentials, the solutions were deoxygenated by passage of a stream of nitrogen through the solution.

Hypobromous acid was prepared by vacuum-distillation of bromine water treated with an excess of silver nitrate, with exclusion of light.

Wellington City Council Laboratory,
City Engineer's Department,
Wellington, New Zealand.

[*Received, November 3rd*, 1959.]

---

600. *The Cleavage of Unsymmetrical Organolead Compounds by Silver Ions.*

By F. Glockling and D. Kingston.

The reactions between silver ions and a series of unsymmetrical organolead compounds of the type Et_3PbR involves cleavage of the R group. Except in those cases (methallyl, benzyl) in which the radical R is resonance-stabilised, there is evidence for unstable organosilver, AgR, compounds which subsequently decompose to silver and the organic free radical.

The behaviour of several symmetrical tetra-alkyl and -aryl derivatives of lead towards silver ions has been reported.[1,2] The primary products are thermally unstable organosilver compounds apparently resulting from cleavage of one organic radical by a single electron-transfer reaction: $R_4Pb + Ag^+ \longrightarrow R_3Pb^+ + RAg$. Even at low temperatures, sometimes at −60°, these coloured organosilver compounds decompose to silver and organic products which could only result from the dimerisation and hydrogen-abstraction reactions of organic free radicals. For example, tetramethyl-lead yields ethane, tetraethyl-lead a mixture of ethane, ethylene, and butane,[1,2] and tetraphenyl-lead gives diphenyl in 74% yield.[3]

Only one unsymmetrical lead alkyl has been studied in this connection,[4] namely, triethylisobut-1-enyl-lead, which undergoes cleavage exclusively of the isobut-1-enyl group on reaction with silver ions in ethanol solution, with formation of isobut-1-enylsilver: $Et_3Pb{\cdot}CH{:}CMe_2 + Ag^+ \longrightarrow Et_3Pb^+ + Me_2C{:}CHAg$. Subsequent decomposition

[1] Semmerano, Riccoboni, *et al.*, *Ber.*, 1941, **74**, 1089, 1297.
[2] Bawn and Whitby, *Discuss. Faraday Soc.*, 1947, **2**, 228.
[3] Gilman and Woods, *J. Amer. Chem. Soc.*, 1943, **65**, 435.
[4] Glockling, *J.*, 1955, 716; 1956, 3640.

of isobut-1-enylsilver affords silver and organic products derived from the isobut-1-enyl radical: $Me_2C{:}CHAg \longrightarrow Me_2C{:}CH\cdot \longrightarrow (Me_2C{:}CH{-})_2 + Me_2C{:}CH_2$.

We now describe the reaction of silver nitrate with further organolead compounds Et_3PbR, the nature of the radical R having been varied with the object of investigating (*a*) the factors which influence the stability of the organosilver primary product R·Ag, and (*b*) the reason for the cleavage of the R–Pb bond rather than the Et–Pb bond. The following compounds, most of which are new, were studied: Triethyl-2-methylprop-2-enyl-lead, $Et_3Pb{\cdot}CH_2{\cdot}C(CH_3){:}CH_2$ (I); Benzyltriethyl-lead, $Et_3Pb{\cdot}CH_2Ph$ (II); Triethyl-*p*-trifluoromethylphenyl-lead, $Et_3Pb{\cdot}C_6H_4{\cdot}CF_3(p)$ (III); *p*-Dimethylaminophenyltriethyl-lead, $Et_3Pb{\cdot}C_6H_4{\cdot}NMe_2(p)$ (IV); Triethyl-α-styryl-lead, $Et_3Pb{\cdot}CH{:}CHPh$ (V).

For each compound reaction with an equivalent or excess of silver nitrate in ethanol resulted in exclusive cleavage of the unsymmetrical group, since in no case were C_2 or C_4 hydrocarbons formed. For the fluoro-compound (III) and the methiodide of the amine (IV) this result was rather surprising since the primary reaction was considered to involve attack by an Ag^+ ion on the most negative carbon atom, in these two cases presumed to be one of the ethyl groups. However, the high polarisability of the lead atom would probably result in the removal of any positive charge from an adjacent carbon atom and the course of the reaction might then be governed by steric factors. (In general, electrophilic substitution reactions occur far more readily at an aromatic than an aliphatic centre.)

Some idea of the relation between the stability of an organosilver compound and the nature of the organic group has emerged from the behaviour of the five compounds. The simple alkyls of silver decompose rapidly at −50°, but isobut-1-enylsilver was stable for several days below −30°. The propenyl compound (I), which should give the isomeric resonance-stabilised isobut-2-enyl (methallyl) radical on decomposition with silver ions, showed no indication of an intermediate organosilver compound. At all temperatures above −100° formation of silver was immediate and 2,5-dimethylhexa-1,5-diene was isolated in 96% yield, presumably being formed by the dimerisation of methallyl radicals: $[2CH_2{:}CMe{\cdot}CH{\cdot}_2 \longrightarrow (CH_2{:}CMe{\cdot}CH_2{-})_2]$. In the case of benzyltriethyl-lead (II) the same general result was observed, *viz.*, no intermediate formation of benzylsilver, but dibenzyl was isolated in high yield, evidently having been formed by dimerisation of the resonance-stablised benzyl radicals. All other cases investigated showed at least signs of the intermediate formation of coloured organosilver compounds. In general it appears that the greater the stability of the radical R, the lower is the stability of the organosilver compound, and in the two extreme cases of methallyl and benzyl, no silver compounds are formed, at least under the conditions of these experiments.

The abnormally high thermal stability of isobut-1-enylsilver is probably connected not only with the low stability of the isobut-1-enyl radical, but also with the presence of a double bond adjacent to the silver atom. It was therefore expected that styrylsilver would show this enhanced thermal stability to a greater extent. Treatment of triethyl-α-styryl-lead (V) with silver nitrate in ethanol results in the formation of a deep red precipitate of styrylsilver which is stable for several hours in air at room temperature. Complete decomposition to silver requires several days at room temperature or several hours at the boiling point of the solvent. The fate of the styryl group was not satisfactorily resolved; 1,4-diphenylbutadiene was not formed, and only traces of styrene were isolated. Most of the styryl groups formed highly insoluble polymeric material.

Experimental

Identification and isolation of triethyl-lead nitrate and of gaseous and volatile products from reactions between silver nitrate and the various organolead compounds followed closely the earlier procedure.[4] Each reaction between an organolead compound and silver nitrate was shown to polymerise styrene.

Triethyl-2-methylprop-2-enyl-lead (I).—A solution of sodium (9·5 g., 0·413 mole) in liquid ammonia (600 c.c.) was added during 2 min. to a solution of tetraethyl-lead (44 c.c., 0·226 mole)

in dry ether (250 c.c.) at −80° to −100° in a silvered vacuum flask. Ethane was rapidly evolved leaving a yellow solution containing sodiotriethyl-lead.[5] After 1 min., 3-chloro-2-methylpropene (30 c.c., 0·2 mole) in ether (100 c.c.) was added rapidly (1—2 min.) with vigorous stirring. The residue after evaporation of ammonia was extracted with ether and water. Distillation of the dried ether extract gave *triethyl-2-methylprop-2-enyl-lead* (30 g., 43%) as a colourless liquid, b. p. 45—50°/0·1 mm. (Found: C, 33·6; H, 6·5; Pb, 58·6. $C_{10}H_{22}Pb$ requires C, 34·4; H, 6·3; Pb, 59·3%). This material gave ethane, ethylene, and butane on reaction with excess of silver nitrate, corresponding to 4·7% of tetraethyl-lead. Two further vacuum distillations reduced this impurity to 0·6%. Bromination in carbon tetrachloride gave 1,2,3-tribromo-2-methylpropane, b. p. 95°/6 mm. (Found: C, 15·8; H, 2·4; Br, 81·4. Calc. for $C_4H_7Br_3$: C, 16·3; H, 2·4; Br, 81·3%). This alkyl decomposes rapidly in sunlight with the formation of a lead mirror. With solid silver nitrate the reaction is almost explosive.

Benzyltriethyl-lead (II).—Previous preparations have resulted in very poor yield. The following procedure gave a 67% yield. Triethyl-lead chloride (83 g., 0·25 mole) was added to a filtered solution of benzylmagnesium chloride prepared from benzyl chloride (50·6 g.; 0·4 mole) and magnesium (11 g.) in ether (200 c.c.), and the mixture heated under reflux with stirring (nitrogen atmosphere) for 1 hr. Distillation of the ether-extract after hydrolysis gave benzyltriethyl-lead (65 g.) as a pale yellow liquid, b. p. 80°/0·05 mm. (Found: C, 40·6; H, 5·8. Calc. for $C_{13}H_{22}Pb$: C, 40·5; H, 5·8%).

Triethyl-p-trifluoromethylphenyl-lead (III).—This was prepared from *p*-bromobenzotrifluoride (22·5 g.; 0·1 mole), tetraethyl-lead (39·0 g.; 0·12 mole), and sodium (5·5 g., 0·24 mole) in liquid ammonia. Vacuum distillation of the *product*, b. p. 80°/0·06 mm. (yield 14 g., 32%), was always accompanied by slight decomposition to lead (Found: C, 34·5; H, 4·6; F, 12·0; Pb, 47·8. $C_{13}H_{19}F_3Pb$ requires C, 35·5; H, 4·4; F, 13·0; Pb, 47·1%). *p*-Chlorbenzotrifluoride did not react with sodiotriethyl-lead under these conditions.

p-*Dimethylaminophenyltriethyl-lead* (IV).—This was prepared by the liquid-ammonia method described above from *p*-bromo-*NN*-dimethylaniline (40 g., 0·2 mole), tetraethyl-lead (71 g., 0·22 mole), and sodium (10·5 g., 0·46 mole) as a yellow oil (43·0 g., 52%), b. p. 150°/0·06 mm. (Found: C, 40·7; H, 6·4; Pb, 50·4. $C_{14}H_{25}NPb$ requires C, 40·7; H, 6·1; Pb, 50·0%). Although thermally stable to at least 180°, the *compound* slowly decomposed in air at room temperature. Excess of methyl iodide in ether solution gave a *methiodide*, m. p. 131—132° (Found: C, 31·3; H, 4·8. $C_{15}H_{28}NIPb$ requires C, 32·4; H, 5·1%).

Triethyl-α-styryl-lead (V).—This was prepared in 40% yield from 2-bromostyrene (37 g., 0·2 mole), tetraethyl-lead (87·5 g., 0·27 mole), and sodium (13 g., 0·56 mole) in liquid ammonia. Distillation gave *triethyl-α-styryl-lead*, b. p. 94°/10^{-3} mm., as a viscous yellow liquid (Found: C, 41·4; H, 5·6; Pb, 51·2. $C_{14}H_{22}Pb$ requires C, 42·3; H, 5·6; Pb, 52·1%). Decomposition takes place even at −78° with separation of a white solid. For reactions with silver nitrate it was used immediately after distillation. Bromination in carbon tetrachloride led to the isolation of 1,2,2-tribromo-1-phenylethane, b. p. 106—110°/0·1 mm. (Found: C, 28·4; H, 2·2; Br, 69·3. Calc. for $C_8H_7Br_3$: C, 28·2; H, 2·1; Br, 69·7%).

Reactions of Et_3PbR *with Silver Nitrate.*—(a) *Triethyl-2-methylprop-2-enyl-lead.* The lead alkyl (5·3 g.) in ethanol (20 c.c.) was treated with silver nitrate (4·0 g.) in methanol (150 c.c.) at −78°. A black precipitate of silver (91% based on lead alkyl) formed immediately. The reaction mixture, filtered off from silver, was shaken with water and ether. The ether extract was concentrated by fractional distillation and the residual ether separated by fractional condensation in a vacuum apparatus through a trap cooled to −70°. The residue, condensed on excess of 1-naphthyl isocyanate to remove ethanol, gave finally 2,5-dimethylhexa-1,5-diene, b. p. 112°/760 mm., (0·80 g.; 96%) (Found: C, 86·9; H, 12·8. Calc. for C_8H_{14}: C, 87·2; H, 12·8%).

(b) *Benzyltriethyl-lead.* The lead alkyl (2·33 g.) in ethanol (20 c.c.) was added to silver nitrate (1·4 g.) in ethanol (70 c.c.) at −78°. Silver (98·5% based on the lead compound) was formed slowly at this temperature and rapidly when the mixture had warmed to −60°. No volatile hydrocarbons could be detected after 20 hr. at room temperature. Ether-extraction gave dibenzyl (0·49 g., 89%), m. p. and mixed m. p. 52·5°.

(c) *Triethyl-p-trifluoromethylphenyl-lead.* The lead compound (1·0 g.) and silver nitrate (0·4 g.) in ethanol (30 c.c.) showed no sign of reaction at −78°, but on warming to room temperature silver was precipitated (90% recovery) with the formation of a transitory red colour. No volatile hydrocarbons were formed, but a small amount of yellow polymer was isolated.

[5] Gilman and Bindschadler, *J. Org. Chem.*, 1953, **18**, 1675.

(d) p-*Dimethylaminophenyltriethyl-lead.* The lead compound (8·5 g.) and silver nitrate (4·0 g.) in ethanol (200 c.c.) at −78° gave a brown solid which slowly decomposed at room temperature with deposition of silver (110% based on the lead compound). No volatile hydrocarbons were produced, and the solution yielded mainly tars and dimethylaniline (0·25 g., 10%), characterised as the *p*-nitroso-derivative.

The methiodide of *p*-dimethylaminophenyltriethyl-lead (0·61 g.) in ethanol (20 c.c.) was treated with ethanolic silver nitrate (0·372 g.; 2 mol.) at −70°. Silver iodide was immediately precipitated, followed by slow formation of silver. As with the parent compound, no volatile hydrocarbons were formed, and extensive tar formation resulted.

(e) Triethyl-α-styryl-lead (20·0 g.) was added slowly to a solution of silver nitrate (9·0 g.) in ethanol (800 c.c.) at −78°. A deep red precipitate formed and was separated by centrifuging. This material, after being twice washed with cold ethanol, was shown to contain silver as the only metal, and to be free from nitrate (Found: Ag, 56. Calc. for Ag·CH:CHPh: Ag, 51%). Decomposition of the crude styrylsilver by boiling it overnight in ethanol gave silver contaminated with insoluble and evidently polymeric material (10·0 g.). Styrene (0·05 g.) was also isolated as the dibromide.

In separate experiments triethyl-α-styryl-lead was shown to form no volatile hydrocarbons on reaction with silver nitrate; deliberate addition of a small amount of tetraethyl-lead resulted in the formation of ethane, ethylene, and butane.

One of us (D. K.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

THE UNIVERSITY, SOUTH ROAD, DURHAM. [*Received, March 3rd,* 1959.]

---

601. *The Chemistry of Fungi. Part XXXVI.* A Revised Structure for Sclerotiorin.*

By F. M. DEAN, J. STAUNTON, and W. B. WHALLEY.

Unequivocal evidence has been obtained that sclerotiorin contains an acetoxyl group. This fact, together with more detailed studies of the properties of *N*-methylsclerotioramine and of certain spectroscopic data, leads to structure (IIa) for sclerotiorin. The new structure is in complete accord with evidence previously interpreted in terms of structure (Ia).

It has been demonstrated previously that sclerotiorin and its derivatives can be aromatised by reductive extrusion of a $C_2H_2O_2$ residue, as in the conversion [1] of sclerotioramine, $C_{21}H_{24}O_4NCl$, into aposclerotioramine $C_{19}H_{22}O_2NCl$ (XIIa). At that time it appeared that sclerotiorin had lactonic properties but did not contain an acetoxyl group, so the tentative structure (Ia) was advanced,[2] the aromatisation being assumed to involve a breakage of a carbon–carbon bond for which there are numerous precedents. It has now been proved that sclerotiorin does contain an acetoxyl group and that this pigment is correctly represented by structure (IIa).

The orientation and natures of the side-chains R in sclerotiorin (Ia or IIa), tetrahydrosclerotiorin (Ib or IIb), and dihydrosclerotiorin (Ic or IIc) have already been fully defined,[1,3,4] and it has been proved [1,2] that these side-chains are unaffected in the reactions with ammonia (or primary amines) which give the related sclerotioramines by replacement of an ether-oxygen atom. Although this type of replacement is characteristic of pyrones, the oxidation [2] of sclerotioramine to berberonic acid (IV) excludes the presence of a simple

* Part XXXV, *J.*, 1958, 1833.

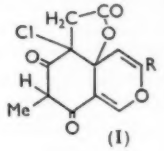
[1] Fielding, Graham, Robertson, Travers, and Whalley, *J.*, 1957, 4931.
[2] Fielding, Robertson, Travers, and Whalley, *J.*, 1958, 1814.
[3] Eade, Page, Robertson, Turner, and Whalley, *J.*, 1957, 4913.
[4] Graham, Page, Robertson, Travers, Turner, and Whalley, *J.*, 1957, 4924.

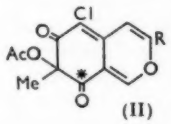
XUM

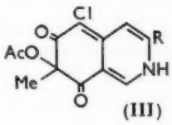
pyrone ring and points to the presence of a vinylogous system (extended pyrone). Moreover, these replacements occur with an ease characteristic of pyrones with acyl rather than alkyl or other substituents,[5] so that partial structures (V) and (VI) are indicated. Either of these would account for the formation of berberonic acid, the tautomeric properties of sclerotioramine [which is amphoteric and gives an *N*-methyl derivative but an *O*-acetate ($\nu_{max.}$ 1770 cm.$^{-1}$)], and the bathochromic shifts in *two* carbonyl frequencies when, for

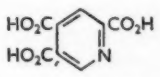
(a) R = ·CH:CH·CMe:CH·CHMeEt (b) R = ·CH_2·CH_2·CHMe·CH_2·CHMeEt

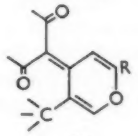
(c) R = ·CH_2·CH_2·CMe:CH·CHMeEt

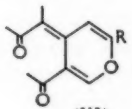

(I)

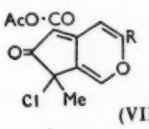

(II)

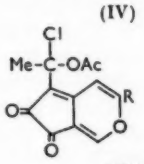

(III)

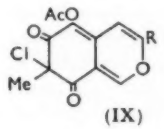

(IV)

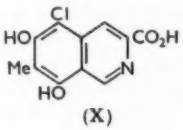

(V)

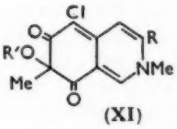

(VI)

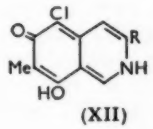

(VII)


(VIII)


(IX)


(X)


(XI)


(XII)

example, tetrahydrosclerotiorin [1718 and 1640 cm.$^{-1}$ (in chloroform)] is converted into tetrahydro-*N*-methylsclerotioramine [1688 and 1600 cm.$^{-1}$ (in chloroform)].

Arrangements must now be made to accommodate in partial structures (V) and (VI) an acetoxyl group, a chlorine atom, and a methyl group which appears as acetic acid in Kuhn–Roth estimations [6] and is attached to carbon in a variety of degradation products, *e.g.*, aposclerotioraminic acid (X). Though there are many possibilities, some, *e.g.*, (VII), can be dismissed at once because sclerotiorin is obviously neither an acid chloride nor an acid anhydride, and others, *e.g.*, (VIII), can be eliminated because it is shown in the sequel that *N*-methylsclerotioramine on hydrolytic deacetylation gives an alcohol which does not easily lose hydrogen chloride, thus proving that the chlorine atom and the acetoxyl group are not attached to the same carbon atom. Of the two surviving structures, (II) and (IX), the latter can be eliminated on the grounds that the chlorine atom appears to be vinylic since it is unreactive except in conditions leading to deep-seated changes, and that the deacetylation referred to above gives an alcohol and not an enol. The conclusion that sclerotiorin has structure (IIa) is very strongly supported by the degradation [2] of sclerotioramine to aposclerotaminic acid (X), the structure of which has recently been rigidly established: [7] the opinion [2] expressed earlier, that the aromatisations do not involve skeletal rearrangements, is also justified.

It is now necessary to show that structure (IIa) accounts satisfactorily for the chief chemical properties of sclerotiorin.

[5] Ost and Reibstein, *J. prakt. Chem.*, 1881, **24**, 284; Wiley and Slaymaker, *J. Amer. Chem. Soc.*, 1956, **78**, 2393.
[6] Birch, Fitton, Pride, Ryan, Smith, and Whalley, *J.*, 1958, 4576.
[7] Staunton and Whalley, unpublished work.

That reductive aromatisation of sclerotiorin and its derivatives is necessarily effected by expulsion of a $C_2H_2O_2$ residue has always been recognised,[2,8] but the identity of this residue has been obscured by the difficulty that, on the one hand, acetic acid might be produced by retro-aldol condensations and, that on the other, formic acid has frequently been the only simple acid detectable in complex hydrolysates. Conditions are now described in which acetic acid can invariably be detected after alkaline hydrolysis of sclerotiorin. It is fortunate that, while sclerotiorin is rapidly destroyed by alkaline hydrolysis, *N*-methylsclerotioramine (IIIa; NMe for NH) is stable enough to permit selective deacetylation, giving an alcohol (XIa; R′ = H) having $\nu_{max.}$ ~3300 cm.$^{-1}$ but bereft of the ester band near 1735 cm.$^{-1}$ which characterises sclerotiorin, *N*-methylsclerotioramine, and their tetrahydro-derivatives. On acetylation, the alcohol regenerates *N*-methylsclerotioramine, so that this compound (and therefore sclerotiorin) must contain an acetoxyl group, and the name *N*-methylisosclerotioramine which was originally applied to the alcohol is now supplanted by deacetyl-*N*-methylsclerotioramine. The formation of aposclerotioramine (XIIa) when sclerotioramine is treated with zinc and alkali and the formation of the resorcinol derivative (XIII) when sclerotiorin is reduced catalytically can of course be regarded as examples of the well-known deacetoxylation of α-acetoxyketones, but a comparison with the behaviour of usnonic acid is much more impressive. Gentle oxidation of usnic acid (XIV) gives usnonic acid (XV) in which the ketol system is sufficiently stable to survive alkaline hydrolysis to the usnetic acid derivative (XVI) but which readily reverts to usnic acid when reduced by zinc.[9]

The formation of an *NO*-dimethyl derivative when sclerotioramine (IIIa) is treated with methyl sulphate and alkali [1] was formerly construed as evidence for a forced enolisation of a β-diketonic system as in (Ia) followed by alkylation. It has now been found that, short of general decomposition, *N*-methylsclerotioramine is not soluble in dilute alkali and cannot be regarded as having either an enolisable system or a lactone ring. As this alkylation cannot be effected in non-hydroxylic solvents and is accompanied by loss of absorption near 1740 cm.$^{-1}$ it must involve hydrolysis of the acetate group followed by methylation of a hydroxyl group activated by two flanking carbonyl groups. This ether is therefore not *NO*-dimethylsclerotioramine but deacetyl-*NO*-dimethylsclerotioramine (XIa; R′ = Me), its stability to dilute acids confirming the view that the hydroxyl group concerned is not enolic. The new structure also explains the production of *N*-methylaposclerotioramine (XIIa; NMe for NH) with zinc and alkali: [1] an enolic ether derived from (Ia) should have yielded an ether of *N*-methylaposclerotioramine. Similarly, tetrahydrosclerotioramine gives deacetyltetrahydro-*NO*-dimethylsclerotioramine (XIb; R′ = Me) and not tetrahydro-*NO*-dimethylsclerotioramine.

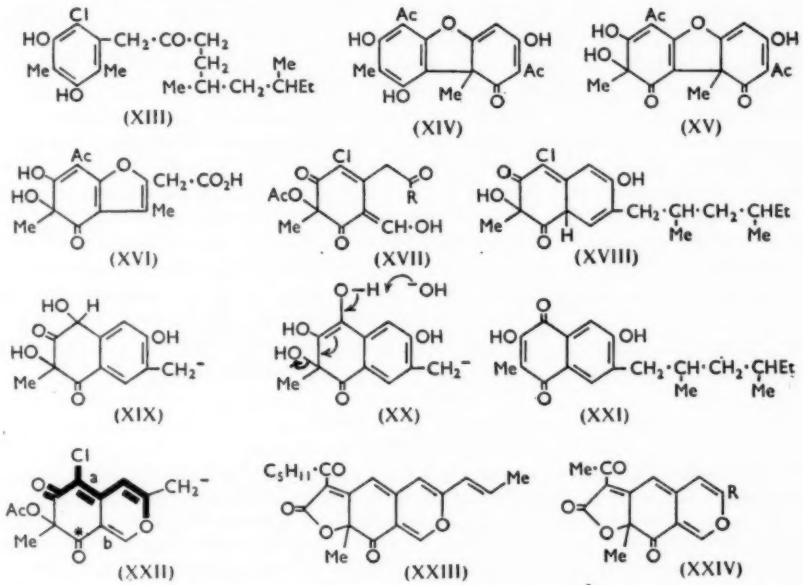
The genesis of the naphthaquinone (XXI) when tetrahydrosclerotiorin (IIb) is attacked by alkali can also be simply explained. That sclerotiorin itself dissolves in dilute sodium hydroxide and is regenerated in part by immediate acidification must now be attributed, not to the presence of a lactone ring, but to fission of the heterocyclic ring giving the enolic system (XVIIa), which eventually suffers further degradation. This interpretation is supported by the ease with which sclerotiorin forms an adduct with aniline,[3] a reaction typical of pyrones: the adduct can be represented by structure (XVIIa; NHPh for OH) in conformity with the spectroscopic properties and with the ready conversion into *N*-phenylsclerotioramine (IIIa; NPh for NH). As explained previously,[4] a similar alkaline fission of tetrahydrosclerotiorin prepares for an aldol condensation resulting in a new carbocyclic ring as in (XVIII). Aromatisation of this by a prototropic shift would give a benzyl chloride, immediate hydrolysis of which would afford a phenolic alcohol (XIX). This would enolise and suffer dehydration to the naphthaquinone (XXI) as indicated in (XX). Dihydrosclerotiorin (IIc) gives a similar naphthaquinone.

The spectroscopic properties of sclerotiorin and its derivatives can also be rationalised

[8] Birkinshaw, *Giorn. Microbiol.*, 1956, **2**, 116.
[9] Asahina and Yanagita, *Ber.*, 1938, **71**, 2260.

XUM

in terms of structure (IIa). The strong absorption at about 1730—1740 cm.$^{-1}$ of sclerotiorin, tetrahydrosclerotiorin, sclerotioramine, and related compounds is more in accord with the acetate structure (IIa) than with the strained γ-lactonic structure (Ia). Sclerotiorin and its hydro-derivatives (IIb and IIc) also absorb near 1715 and 1640 cm.$^{-1}$: the latter band is very intense and very complex so that it can be attributed to an extensively conjugated carbonyl group, but the former band seems to support a cyclopentenone grouping as in (VII) or (VIII). However, models make it clear that the strain imposed by the one tetrahedral carbon atom in the otherwise planar cyclic system of (IIa) can be relieved by twisting one carbonyl group out of the plane and therefore (to some extent) out of conjugation: the affected group might then absorb near 1715 cm.$^{-1}$. This group must be that starred in (IIa), otherwise it would be difficult to account for conjugated



carbonyl absorption as low as 1640 cm.$^{-1}$, and it is in any case improbable that the longer conjugated system would be disrupted in preference to the shorter. It must be noted that reduced conjugation in the starred carbonyl group does not vitiate the argument advanced at the beginning for the presence of an acylpyrone system, because the inductive effect alone would still constitute effective activation: in contrast, the argument would have collapsed had the other carbonyl group been displaced.

It is difficult to interpret the ultraviolet spectra of cross-conjugated systems as complex as that in sclerotiorin (IIa), but the spectrum of tetrahydrosclerotiorin (IIb) can be dealt with approximately. Again it seems that the carbonyl group starred in (II) is not effectively conjugated. Selective absorption at the longest wavelength should be defined by the system heavily marked in (XXII): the alternative system constructed with the ethylenic bond (b) would absorb at shorter wavelengths because the olefinic link (a) is now *cis*-orientated and because even a non-conjugated carbonyl group attached to (b) would reduce the π-electron mobility still further, so this system can be ignored. The parent dienone would have [10] $\lambda_{max.}$ 260 mμ, which, with increments of +20 for the two substituents

[10] Data from Braude and Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, New York, 1955.

(Cl and R), +5 (exocyclic double bond), and +50 (auxochromic oxygen atom), suggests that tetrahydrosclerotiorin should have $\lambda_{max.}$ 335 mμ. This is reassuringly close to the observed value of 343 mμ, and, since the oxygen atom exerts its full auxochromic effect, it confirms the view that the starred carbonyl group is not fully conjugated. Had the other carbonyl group been displaced instead, it would have been very difficult indeed to account for intense absorption beyond about 270 mμ. The auxochromic effect of dialkylamino being ~95 mμ, a similar calculation * gives $\lambda_{max.}$ 380 mμ for tetrahydro-*N*-methylsclerotioramine (IIIb), the observed value being 381 mμ.

The lead tetra-acetate oxidation of phenols, extensively studied by Wessely and his collaborators,[11] gives acetoxycyclohexenones similar to sclerotiorin (IIa). When tetrahydro-*N*-methylaposclerotioramine (XIIb; NMe for NH) was oxidised in this way, a fair yield was obtained of a substance having the general properties of tetrahydro-*N*-methylsclerotioramine (IIIb; NMe for NH): indeed, the two materials were spectroscopically indistinguishable. Although the stereochemical complexity of the side-chain [3] and the lack of stereospecificity at the point of oxidation prevented complete identification, the nature of the reaction clearly supports structure (IIa) for sclerotiorin most strongly.

On the basis of structure (IIa), sclerotiorin is formed from a linear sequence of eight acetate units with the incorporation of three other carbon atoms, an acetoxyl group, and a chlorine atom. This accords most satisfactorily with the biogenetical evidence.[6] Finally, rubropunctatin (an extended pyrone closely similar to sclerotiorin and obtained from *Monascus rubropunctatus* Sâto) is regarded by Haws, Holker, and Kelly [12] as having structure (XXIII) and they have pointed out to us that, in the light of the revised structure for sclerotiorin, rubropunctatin can be envisaged as being biogenetically derived from a precursor similar to deacetylsclerotiorin by esterification of the tertiary hydroxyl group with β-oxo-octanoic acid followed by aldol condensation and dehydration: since rotiorin [13] is a co-pigment of sclerotiorin in *Penicillium sclerotiorum* van Beyma, similar arguments are applicable and lead to structures of type (XXIVa) for this compound.

Experimental

Alkaline Degradation of Sclerotiorin.—Sclerotiorin (2 g.) slowly dissolved when warmed on the steam-bath during 1½ hr. with 2N-sodium hydroxide solution (50 ml.). The cooled hydrolysate was acidified with excess of 2N-sulphuric acid, filtered, diluted with distilled water, and steam-distilled until the condensate was neutral. Titration with 0·1N-sodium hydroxide indicated that the total water-soluble, steam-volatile acid was equivalent to 1·59 mol.

The neutralised solution was concentrated to approx. 100 ml. and boiled for 1 hr. with an excess of 0·1N-aqueous potassium permanganate containing an excess of sodium hydrogen carbonate; then the cooled reaction mixture was acidified with 2N-sulphuric acid, filtered to remove manganese dioxide, and again steam-distilled. Titration of the distillate as above indicated the presence of 1·01 mol. of a steam-volatile acid (presumably acetic acid). Evaporation of the neutralised distillate to dryness, followed by conversion into the benzimidazole in the usual manner, gave 2-methylbenzimidazole (0·2 g.), m. p. and mixed m. p. 177° (mixed m. p. with benzimidazole *ca.* 160°). No other product could be detected.

Deacetyl-N-methylsclerotioramine.—The following improved method was used for the preparation of this compound. A solution of 2N-sodium hydroxide (5 ml.) was added to *N*-methylsclerotioramine (1 g.) in alcohol (20 ml.), and 90 seconds later the mixture was poured into water (200 ml.). The resulting precipitate was extracted with chloroform (4 × 20 ml.). The washed and dried extract was purified by chromatography on neutralised aluminium oxide and the eluate evaporated *in vacuo*, to furnish *deacetyl-N-methylsclerotioramine* which separated

* It will be noted that the double bond (b) is not regarded as a substituent. Justification for this rests partly on general grounds but mainly on the fact that with citrinin, which contains a similar grouping, calculations are successful only if an equivalent assumption is made.

[11] Wessely and Sinwel, *Monatsh.*, 1950, **81**, 1055, and subsequent papers.
[12] Haws, Holker, and Kelly, personal communication.
[13] Jackman, Robertson, Travers, and Whalley, *J.*, 1958, 1825.

from aqueous methanol in violet needles (0·35 g.), m. p. 160—165° (decomp.) (Found: C, 65·9; H, 6·7; N, 3·5. $C_{20}H_{24}O_3NCl$ requires C, 66·6; H, 6·7; N, 3·9%).

Reacetylation of this compound (0·35 g.) in acetic anhydride (2 ml.) containing toluene-*p*-sulphonic acid (0·3 g.) during 18 hr. at room temperature gave *N*-methylsclerotioramine (0·21 g.) in red needles (from methanol), m. p. and mixed m. p. 230—231° (decomp.), having the requisite infrared spectrum (Found: C, 65·2; H, 6·5; N, 3·4. Calc. for $C_{22}H_{26}O_4NCl$: C, 65·5; H, 6·5; N, 3·5%). This substance exhibited the characteristic dimorphism: [1] on recrystallisation from aqueous methanol the red needles were converted quantitatively into the violet modification, m. p. and mixed m. p. 230° (decomp.), having the requisite infrared spectrum; the reverse transformation was also readily effected.

The infrared spectra of these two modifications are identical when determined for chloroform solutions. But contrary to our previous report [1] the spectra are not identical when determined in Nujol. When a machine of greater resolving power than that previously available to us was used, slight differences in the 10—13·5 mμ region of the spectrum were observed.

C-Methyl estimations upon tetrahydro- and deacetyltetrahydro-*N*-methylsclerotioramine were not significantly different.

Deacetyltetrahydro-NO-*dimethylsclerotioramine*.—The method previously described [1] for the preparation of this compound has been modified as follows. Dimethyl sulphate (2 ml.) was added to a vigorously agitated solution of tetrahydrosclerotioramine (1 g.) in 2N-sodium hydroxide (50 ml.), and the oily product which separated during 10 min. was isolated with chloroform (50 ml.). After dilution with light petroleum (b. p. 60—80°) (100 ml.) the extract was chromatographed on neutralised aluminium oxide when *deacetyltetrahydro*-NO-*dimethylsclerotioramine* was eluted with chloroform–light petroleum (b. p. 60—80°) (1 : 2) and separated from methanol in red plates (0·3 g.), m. p. 201° (decomp.) [the previously recorded m. p. was 188° (decomp.)] (Found: C, 66·6; H, 8·1; OMe, 7·7. $C_{20}H_{27}O_2NCl{\cdot}OMe$ requires C, 66·5; H, 7·9; OMe, 8·2%).

Acetoxylation of Tetrahydro-N-*methylaposclerotioramine*.—When lead tetra-acetate (1 g.) was added to a solution of tetrahydro-*N*-methylaposclerotioramine (1 g.) in acetic acid (20 ml.) the oxidising agent rapidly dissolved, the solution darkened, and after 15 min. crystals separated. 24 hr. later the mixture was diluted with water (100 ml.), and the red-brown precipitate extracted with chloroform. Purification of this extract by chromatography on neutralised aluminium oxide gave a product, which separated from aqueous methanol in orange plates (0·2 g.), m. p. 198° (decomp.) and mixed m. p. 201° (decomp.) (Found: C, 64·8; H, 7·3. Calc. for $C_{22}H_{30}O_4NCl$: C, 64·7; H, 7·2%). This compound is indistinguishable from tetrahydro-*N*-methylsclerotioramine by means of the crystalline form, solubility in the usual organic solvents, or infrared spectrum or ultraviolet spectrum.

Aniline Adduct of Sclerotiorin.—This compound has $\lambda_{max.}$ 228, 285, and 365 mμ (log ε 4·2, 4·3, and 4·5 respectively) and $\nu_{max.}$ 1727 (s) (acetate), 1692 (s), 1661 (s), 1637 (s), and 1621 (s) cm.$^{-1}$.

The ultraviolet absorption spectra were measured for 95% alcohol solutions with a Unicam S.P. 500 Spectrophotometer, and the infrared spectral data were obtained on a Perkin-Elmer, Model 21, Spectrophotometer by Mr. J. V. Barkley. The analyses were by Mr. C. Tomlinson and Mr. D. Newman and their associates of this Department.

UNIVERSITY OF LIVERPOOL.

[*Received, March 30th*, 1959.]

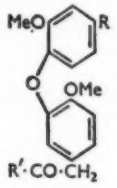
602. *Bisbenzylisoquinolines. Part III.*[1] *The Synthesis of Isoquinoline Intermediates.*

By M. F. Grundon.

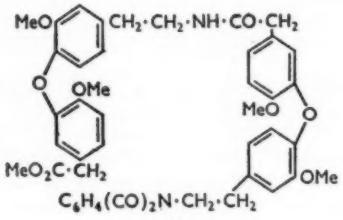
The amide (II) was prepared by reaction of 5′-chlorocarbonylmethyl-2,2′-dimethoxy-4-(2-phthalimidoethyl)diphenyl ether with 4-(2-aminoethyl)-2,2′-dimethoxy-5′-methoxycarbonylmethyldiphenyl ether. Cyclisation gave the 3,4-dihydroisoquinoline [III; R = $CH_2{\cdot}N(CO)_2C_6H_4$-*o*], which was converted into the corresponding tetrahydro-2-methylisoquinoline (V).

One approach to the synthesis of unsymmetrical cyclic bisbenzylisoquinoline alkaloids such as tubocurarine chloride involves condensation of amino-acids containing the diphenyl ether structure, followed by cyclisation. This method has been explored by using the amino-acid (I; R = $CH_2{\cdot}CH_2{\cdot}NH_2$, R′ = OH).[2]

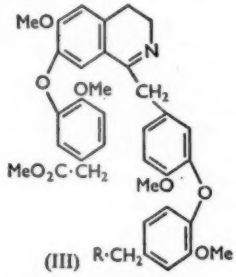
The amino-ester (I; R = $CH_2{\cdot}CH_2{\cdot}NH_2$, R′ = OMe) was prepared by esterification of the acid, and characterised as its *N*-phthaloyl derivative, obtained for comparison by the reaction of the *N*-phthaloyl acid [I; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = OH] with diazomethane. The phthalimido-acid chloride [I; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = Cl] and the amino-ester afforded the crystalline amide (II) in almost quantitative yield.



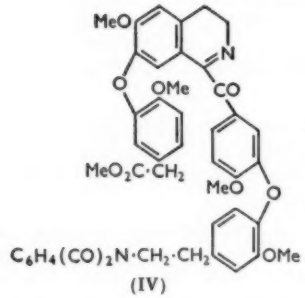
(I)



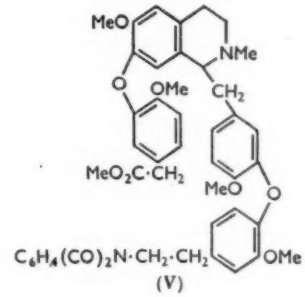
(II)



(III)



(IV)



(V)

Attempts to prepare amides from the amino-acid failed. Thus, the acid chloride and the amino-acid gave a product difficult to purify, which with diazomethane afforded the amide (II) in only poor yield.

The amino-acid did not react with the mixed anhydride derived from the phthalimido-acid and methyl chloroformate. The only product isolated was the methyl phthalimido-ester [I; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R′ = OMe], formed apparently by decomposition of the intermediate anhydride.

[1] Part II, Crowder, Grundon, and Lewis, *J.*, 1958, 2142.
[2] Grundon and Perry, *J.*, 1954, 3531.

When heated with phosphorus oxychloride, the amide (II) was converted into the 3,4-dihydroisoquinoline [III; R = CH_2·N$(CO)_2C_6H_4$-*o*], isolated as the picrate (75%). The amide and phosphorus pentachloride at room temperature gave a compound containing chlorine. Its structure has not been established, but it is apparently neither a hydrochloride nor an imino-chloride as it is unaffected by cold sodium hydroxide.

The 3,4-dihydroisoquinoline, like 1-benzyl-3,4-dihydroisoquinoline,[3] is autoxidised in ethanol to the 1-benzoyl-3,4-dihydroisoquinoline (IV).

The crude benzyldihydroisoquinoline, recovered rapidly from its picrate, gave a methiodide, which, although not crystalline, was shown by its infrared spectrum to resist atmospheric oxidation. Catalytic reduction of the methiodide in the presence of diethylamine afforded the 1,2,3,4-tetrahydro-2-methylisoquinoline (V), isolated as its picrate.

Reduction of the methiodide with sodium borohydride was unsatisfactory. The product was not characterised, but its infrared spectrum suggested that the alkaline conditions had caused partial hydrolysis of the phthaloyl group. Reaction of the phthalimido-ester [I; R = CH_2·CH_2·N$(CO)_2C_6H_4$-*o*, R′ = OMe] with sodium borohydride resulted in hydrolysis of the ester and *N*-phthaloyl groups: the product did not depress the melting point of the phthalimido-acid [I; R = CH_2·CH_2·N$(CO)_2C_6H_4$-*o*, R′ = OH], but the two compounds were not identical (infrared; Table); the product is apparently the phthalamic acid, which undergoes ring closure on heating. *N*-(3,4-Dimethoxyphenylethyl)phthalimide was unaffected by sodium borohydride: brief alkaline hydrolysis afforded the phthalamic acid.

An alternative synthesis was explored, using a nitrile group as a potential amino-group. 5′-Carboxymethyl-4-formyl-2,2′-dimethoxydiphenyl ether[2] was converted into the nitrile (I; R = CH_2·CN, R′ = OH) by the rhodanine method. Catalytic reduction of this nitrile is a more satisfactory method of preparing the amino-acid (I; R = CH_2·CH_2·NH_2, R′ = OH) than that recorded previously.[2] Without purification of intermediates, the nitrile was converted into its acid chloride and condensed with the amino-ester (I; R = CH_2·CH_2·NH_2, R′ = OMe), and the resultant amide cyclised with phosphorus oxychloride to the 3,4-dihydroisoquinoline (III; R = CH_2·CN), obtained as its picrate. The approach is not promising, as the yield is poor and reduction of the dihydroisoquinoline nitrile failed to give a characterisable product.

Assignment of infrared absorption bands (KBr *disc*) *in the region* 1800—1620 *cm.*$^{-1}$.

Substance *	*N*-Phthaloyl	CO_2Me	CO_2H	Amide	Others
(I; R = CH_2·CH_2·NH_2, R′ = OH)	—	—	—	—	1570 s (CO_2^-)
(I; R = CH_2·CH_2·NPT, R′ = OH)	1770 w, 1716 s	—	—	—	
(I; R = CH_2·CH_2·NPT, R′ = OMe)	1764 w, 1710 s	1736 m	—	—	
(II)	1768 w, 1705 s	1734 m	—	1673 m	
Hydrochloride of (III; R = CH_2·NPT)	1770 w, 1710 s	—	—	—	1650 m (–C=$\overset{+}{N}$H–)
(IV)	1765 w, 1708 s	1730 m	—	—	1667 m (–CO–$\overset{\vert}{C}$=N–)
Methiodide of (III; R = CH_2·NPT)	1770 w, 1715 s	—	—	—	
(V)	1757 w, 1700 s	1725 m	—	—	
Product from methiodide of (III; R = CH_2·NPT) + $NaBH_4$	—	1735 m	1700 m	1685 m	
Product from (I; R = CH_2·CH_2·NPT, R = OMe) + $NaBH_4$	—	—	1720 m, 1700 m	1667 s	
N-(2-3′,4′-Dimethoxyphenylethyl)phthalimide	1755 m, 1700 s	—	—	—	
Product from hydrolysis of preceding imide ...	—	—	1718 s	1625 s	

* PT = *o*-$C_6H_4(CO–)_2$

The compounds of high molecular weight reported in this paper are not always characterised uniquely by analytical results. Infrared evidence is summarised in the Table.

[3] See, for example, Buck, Haworth, and Perkin, *J.*, 1924, 2176; Clemo and Temple, *J.*, 1953, 678.

Experimental

5'-Chlorocarbonylmethyl-2,2'-dimethoxy-4-(2-phthalimidoethyl)diphenyl Ether [I; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R' = Cl].—5'-Carboxymethyl-2,2'-dimethoxy-4-(2-phthalimidoethyl)-diphenyl ether (0·45 g.), phosphorus pentachloride (0·45 g.), and benzene (10 c.c.) were heated under reflux for 15 min. The cold solution deposited the *acid chloride* (0·38 g.), crystallising from benzene–light petroleum (b. p. 60—80°) in prisms, m. p. 142—144° (Found: C, 65·6; H, 4·7. $C_{26}H_{22}O_6NCl$ requires C, 65·1; H, 4·6%).

N-[4-Methoxy-3-(2-methoxy-4-2'-phthalimidoethylphenoxy)phenyl]acetyl-2-[3-methoxy-4-(2-methoxy-5-methoxycarbonylmethyl)phenoxy]ethylamine (II).—(*a*) A solution of 5'-chlorocarbonylmethyl-2,2'-dimethoxy-4-(2-phthalimidoethyl)diphenyl ether (0·4 g.) in chloroform (10 c.c.) was added during 30 min. to a solution of 4-(2-aminoethyl)-2,2'-dimethoxy-5'-methoxycarbonylmethyldiphenyl ether (0·29 g.) and tributylamine (0·25 g.) in chloroform (10 c.c.). After 12 hr. the solution was washed with N-hydrochloric acid, N-sodium hydroxide, and water. Evaporation gave a gum, which was triturated with N-hydrochloric acid and water. Crystallisation from methanol afforded the *amide* (0·6 g., 91%), m. p. 70—77°. A sample separated from methanol in aggregates of fine needles, m. p. 80—81° (Found: C, 68·2; H, 5·5. $C_{45}H_{44}O_{11}N_2$ requires C, 68·5; H, 5·6%).

(*b*) A solution of 5'-chlorocarbonylmethyl-2,2'-dimethoxy-4-(2-phthalimidoethyl)diphenyl ether (0·35 g.) in aqueous dioxan was added during 45 min. to a solution of 4-(2-aminoethyl)-5'-carboxymethyl-2,2'-dimethoxydiphenyl ether (0·17 g.) in aqueous dioxan containing sodium carbonate (0·03 g.). The solution was kept alkaline by the periodic addition of aqueous sodium carbonate. After 1 hr. the solution was acidified with hydrochloric acid. Chloroform extraction gave a gum (0·35 g.), $\lambda_{max.}$ (in KCl) 1775 m, 1710 s, 720 s cm.$^{-1}$.

A portion of the gum, when esterified with diazomethane, gave the ester, separating from methanol in needles, m. p. 72—75°, not depressed by mixing with a sample prepared in (*a*).

2,2'-Dimethoxy-5'-methoxycarbonylmethyl-4-(2-phthalimidoethyl)diphenyl Ether [I; R = $CH_2{\cdot}CH_2{\cdot}N(CO)_2C_6H_4$-*o*, R' = OMe].—(*a*) A solution of 4-(2-aminoethyl)-5'-carboxymethyl-2,2'-dimethoxydiphenyl ether (0·17 g.) in water (3 c.c.) was added to a solution of 5'-carboxymethyl-2,2'-dimethoxy-4-(2-phthalimidoethyl)diphenyl ether (0·17 g.) in dioxan (3 c.c.) containing methyl chloroformate (0·05 g.) and tributylamine (0·08 g.) at 0°. After 30 min. the solution was diluted with water and acidified with hydrochloric acid. The precipitate of the *ester* crystallised from ethanol in needles (0·13 g.), m. p. 146—150°, raised to 158—159° by recrystallisation (Found: C, 68·6; H, 5·4; N, 3·1. $C_{27}H_{25}O_7N$ requires C, 68·2; H, 5·3; N, 3·0%).

(*b*) 5-Carboxymethyl-2,2'-dimethoxy-4-(2-phthalimidoethyl)diphenyl ether (0·1 g.) in acetone–methanol was treated with ethereal diazomethane. After 15 min. the solution was evaporated. The residue crystallised from methanol in needles (0·095 g.), m. p. and mixed m. p. 156—157°.

(*c*) A solution of 4-(2-aminoethyl)-5'-carboxymethyl-2,2'-dimethoxydiphenyl ether (50 mg.) and concentrated sulphuric acid (1 c.c.) in methanol (20 c.c.) was kept for 12 hr. The residue obtained by evaporation was dissolved in water, made alkaline with sodium carbonate, and extracted with chloroform. Evaporation of the chloroform gave an oil. Heating this with phthalic anhydride (30 mg.) at 140—150° for 1 hr. gave the methyl ester, needles (from methanol), m. p. and mixed m. p. 154—156°.

Picrate of 3,4-Dihydro-6-methoxy-7-(2-methoxy-5-methoxycarbonylmethylphenoxy)-1-[4-methoxy-3-(2-methoxy-4-2'-phthalimidoethylphenoxy)benzyl]isoquinoline [III; R = $CH_2{\cdot}N(CO)_2C_6H_4$-*o*].—The amide (II) (0·37 g.), toluene (20 c.c.), and phosphorus oxychloride (2 c.c.) were heated under reflux for 30 min. Evaporation, addition of water, and extraction with chloroform afforded a gum, which was triturated with toluene, to give the crude hydrochloride (for infrared spectrum see Table). A solution of the hydrochloride in warm ethanol (30 c.c.) was allowed to cool, filtered from insoluble material, and treated with excess of picric acid in ethanol. The *picrate* crystallised from methanol as a yellow solid (0·34 g., 75%). A sample separated from methanol in yellow prisms, m. p. 178—179° (Found: C, 61·3; H, 4·8; N, 7·1. $C_{51}H_{45}O_{17}N_5$ requires C, 61·2; H, 4·6; N, 7·0%).

3,4-Dihydro-6-methoxy-7-(2-methoxy-5-methoxycarbonylmethylphenoxy)-1-[4-methoxy-3-(2-methoxy-4-2'-phthalimidoethylphenoxy)benzoyl]isoquinoline (IV).—A solution of the above picrate (90 mg.) in chloroform was shaken with several portions of aqueous sodium carbonate and

evaporated. Crystallisation of the residue from ethanol gave the benzoyl compound in aggregates of needles (25 mg.), m. p. 101—103° (Found: C, 67·2; H, 5·4. $C_{45}H_{40}O_{11}N_2,1H_2O$ requires C, 67·3; H, 5·3%). A solution of the compound in acetic anhydride became blue-green when heated. The *picrate* had m. p. 110—114° (from ethanol) (Found: C, 59·8; H, 4·4; N, 6·8. $C_{51}H_{43}O_{18}N_5$ requires C, 60·4; H, 4·3; N, 6·9%).

Reaction of the Amide (II) *with Phosphorus Pentachloride.*—A solution of the amide (280 mg.) in chloroform (10 c.c.) was treated with phosphorus pentachloride (300 mg.) and kept for 3 days. The solution was shaken with water, and the chloroform evaporated. Crystallisation of the residue from methanol gave a white *product* (180 mg.), m. p. 100—102° (Found: C, 65·6; H, 5·5; Cl, 4·5. $C_{45}H_{43}O_{10}N_2Cl,1H_2O$ requires C, 65·7; H, 5·5; Cl, 4·3%).

Picrate of 1,2,3,4-*Tetrahydro*-6-*methoxy*-7-(2-*methoxy*-5-*methoxycarbonylmethylphenoxy*)-1-[4-*methoxy*-3-(2-*methoxy*-4-2′-*phthalimidoethylphenoxy*)*benzyl*]-2-*methylisoquinoline* (V).—The dihydroisoquinoline picrate (270 mg.) was converted into the base by shaking its chloroform solution with aqueous sodium carbonate. A solution of the base in methanol and methyl iodide was refluxed for 1½ hr. Evaporation gave the methiodide as a yellow powder, m. p. 110—114°.

The crude methiodide and diethylamine (0·5 c.c.) in ethanol (100 c.c.) were hydrogenated at room temperature and atmospheric pressure in the presence of platinum oxide (0·5 g.). After removal of the catalyst, the solution was evaporated. A solution of the residue in chloroform was shaken with 2N-sodium hydroxide and water, and evaporated. Trituration of the residue with light petroleum (b. p. 40—60°) gave a colourless solid (160 mg.), converted, in ethanol, into the *picrate* (180 mg.), m. p. 103—105° (from ethanol) (Found: C, 60·3; H, 4·7; N, 7·4. $C_{52}H_{49}O_{17}N_5,1H_2O$ requires C, 60·4; H, 5·0; N, 6·8%).

Reaction of 2,2′-*Dimethoxy*-5′-*methoxycarbonyl*-4-(2-*phthalimidoethyl*)*diphenyl Ether with Sodium Borohydride.*—Sodium borohydride (50 mg.) was added in portions to a solution of the ester (50 mg.) in methanol (30 c.c.). After 10 min. most of the methanol was removed and water was added. Acidification with hydrochloric acid gave an oil which was obtained with chloroform and separated from ethanol in prisms (25 mg.), m. p. 179—180° alone or mixed with 5′-carboxymethyl-2,2′-dimethoxy-4-(2-phthalimidoethyl)diphenyl ether. The infrared spectrum of the product was not identical with that of the phthalimido-acid (Table).

2-(3,4-*Dimethoxyphenyl*)*ethylphthalimide.*—A solution of 2-(3,4-dimethoxyphenyl)ethylamine (1 g.) and phthalic anhydride (0·9 g.) in acetic acid (10 c.c.) was heated on a steam-bath for 2 hr. The solution was diluted with water; the precipitated *phthalimide* separated from methanol in plates, m. p. 173—174° (Found: C, 69·4; H, 5·6. $C_{18}H_{17}O_4N$ requires C, 69·4; H, 5·5%).

Hydrolysis by hot aqueous-ethanolic N-sodium hydroxide gave the *phthalamic acid*, rectangular plates (from ethanol), m. p. 159—161° (Found: C, 65·6; H, 5·8; N, 4·5. $C_{18}H_{19}O_5N$ requires C, 65·7; H, 5·8; N, 4·3%), and, after resolidifying, m. p. 171—172°, not depressed on admixture with the preceding phthalimide.

5′-*Carboxymethyl*-4-*cyanomethyl*-2,2′-*dimethoxydiphenyl Ether* (I; R = CH_2·CN, R′ = OH).—A solution of 5′-carboxymethyl-4-formyl-2,2′-dimethoxydiphenyl ether (9·65 g.), rhodanine (5·0 g.), and anhydrous sodium acetate (10·0 g.) in acetic acid (50 c.c.) was heated under reflux for 30 min. The precipitate of the rhodanine derivative was removed by filtration of the hot mixture. A further quantity was obtained by refluxing the filtrate for 1 hr.

The crude rhodanine derivative (13·1 g.) and aqueous 15% sodium hydroxide (80 c.c.) were heated on a steam-bath for 40 min. The solution at 0° was acidified with dilute hydrochloric acid, and the precipitated thioketo-acid was dried at room temperature.

A solution of the thioketo-acid in ethanol (100 c.c.) containing hydroxylamine [prepared from hydroxylamine hydrochloride (8·6 g.) and sodium (2·7 g.)] was refluxed for 40 min. After the ethanol had been removed, water (100 c.c.) was added, and the solution was acidified with hydrochloric acid. The solution was shaken with ether (40 c.c.), and the hydroxyimino-acid (10·5 g.), m. p. 155—159°, was removed by filtration. By separation of the ether solution and concentration to 5 c.c. a further quantity (0·5 g.) of the hydroxyimino-acid was obtained.

The crude product (11 g.) in acetic anhydride (50 c.c.) was warmed until a clear solution was obtained, then heated on a steam-bath for 20 min., diluted with water (250 c.c.), and set aside for 12 hr. The *nitrile* (6·5 g.), m. p. 154—158°, was obtained by trituration of the precipitate with ethanol. A further quantity (0·25 g.) was obtained from the aqueous solution with chloroform (total yield, 6·75 g., 68%). A sample crystallised from ethanol in rods, m. p. 158—160° (Found: C, 65·9; H, 5·1. $C_{18}H_{17}O_5N$ requires C, 66·1; H, 5·2%).

XUM

4-(2-*Aminoethyl*)-5′-*carboxymethyl*-2,2′-*dimethoxydiphenyl Ether* (I; R = $CH_2 \cdot CH_2 \cdot NH_2$, R′ = OH).—The nitrile (2·2 g.) in acetic acid (150 c.c.) containing platinum oxide (0·6 g.) was hydrogenated at room temperature and atmospheric pressure. When hydrogen absorption ceased (2·5 hr.), the catalyst was removed and the solution evaporated. Crystallisation of the residue from ethanol gave the amino-acid (1·98 g., 90%), m. p. and mixed m. p. 173—174°.

Picrate of* 3,4-*Dihydro*-6-*methoxy*-1-[4-*methoxy*-3-(4-2′-*cyanoethyl*-2-*methoxyphenoxy*)-*benzyl*]-7-(2-*methoxy*-5-*methoxycarbonylmethylphenoxy*)*isoquinoline (III; R = $CH_2 \cdot CN$).—A solution of 5′-carboxymethyl-4-cyanomethyl-2,2′-dimethoxydiphenyl ether (0·75 g.) in thionyl chloride (7 c.c.) was refluxed for 2 hr., and evaporated. The residue in chloroform (20 c.c.) was added during 30 min. to a solution of 4-(2-aminoethyl)-2,2′-dimethoxy-5′-methoxycarbonylmethyldiphenyl ether (0·75 g.) and tributylamine (0·45 g.) in chloroform (20 c.c.). The solution was kept overnight, then evaporated, and the residue was triturated with N-hydrochloric acid (2 × 20 c.c.) and dissolved in chloroform. The solution was shaken with aqueous sodium carbonate and evaporated, giving the amide as a gum (1·15 g.).

A mixture of the crude amide, toluene (20 c.c.), and phosphorus oxychloride (3 c.c.) was heated under reflux for 45 min. The solution was evaporated, and the residue was dissolved in boiling ethanol (60 c.c.) and allowed to cool. The clear solution, obtained by decantation, was treated with excess of picric acid in ethanol. The precipitate of crude *picrate* (0·91 g.), m. p. 89—92°, was extracted with boiling methanol (60 c.c.) and the methanol was removed. The residue separated from acetone–methanol in yellow needles (0·5 g., 25%), m. p. 118—120° and after recrystallisation, m. p. 119—120° (Found: C, 59·9; H, 4·5; N, 8·1. $C_{43}H_{39}O_{15}N_5$ requires C, 59·6; H, 4·5; N, 8·1%).

THE QUEEN'S UNIVERSITY OF BELFAST. [*Received, April 3rd*, 1959.]

---

603. *Oxidations of Organic Compounds with Quinquevalent Vanadium. Part II.*[1] *The Oxidation of Ketones.*

By J. S. LITTLER and WILLIAM A. WATERS.

The oxidations of cyclopentanone and cyclohexanone by quinquevalent vanadium in sulphuric and perchloric acid solutions are first-order reactions in respect to both V^V and the organic substrate. The dependence on acidity in perchloric acid solution can be attributed to oxidation by a yellow cation, probably $V(OH)_3^{++}$, and in sulphuric acid solution to a more active red sulphate complex. There is a large positive salt effect.

Oxygen retards the disappearance of V^V when cyclopentanone is being oxidised, but, though it is absorbed, it has no effect on this rate with cyclohexanone as substrate.

Reaction products have been examined, and it is concluded that oxidations of ketones by V^V involve consecutive one-electron abstraction steps.

IN Part I of this series[1] it was indicated that ketones are oxidised by acid solutions of quinquevalent vanadium with formation of transient organic free radicals. We have now studied kinetically the oxidations of cyclohexanone and cyclopentanone using both sulphuric and perchloric acid and have elucidated somewhat further the nature of the oxidising species. The investigation also sheds some light on the mechanism of the oxidation.

RESULTS

(1) *Dependence of Rate on Ketone Concentration.*—With both ketones the rate of consumption of V^V is a first-order process with respect to the ketone concentration. The rate is expressed as the pseudo-unimolecular rate constant k obtained from the slope of the graph of log [V^V] against time (see Tables 1 and 2).

[1] Part I, Littler and Waters, *J.*, 1959, 1299.

(2) *Dependence of Rate on* V^V *Concentration.*—As in the experiments described in Part I, oxidations carried out in the presence of excess of the organic compound all gave good first-

TABLE 1. *Oxidation of cyclopentanone in aqueous sulphuric acid: reaction order with respect to ketone, at* 40°.

$[H_3O^+] = 5{\cdot}18$M, $[V^V] = 0{\cdot}0486$N.

[Ketone] (M)	0·121	0·090	0·060	0·030	0·012
10^4k (sec.$^{-1}$)	9·17	7·13	5·09	2·54	1·05
10^3k/[Ketone]	7·5	7·9	8·5	8·5	8·7

Mean value of k/[Ketone] = (8·22 ± 0·4) × 10^{-3} sec.$^{-1}$ mole^{-1}.

TABLE 2. *Oxidation of cyclohexanone in aqueous sulphuric acid: reaction order with respect to ketone, at* 35°.

$[H_3O^+] = 1{\cdot}1$M, $[V^V] = 0{\cdot}0565$N, ionic strength = 1·2M.

[Ketone] (M)	0·1205	0·241	0·3615
10^4k	2·43	4·98	7·35
10^3k/[Ketone]	2·02	2·07	2·04

Mean value of k/[Ketone] = (2·04 ± 0·02) × 10^{-3} sec.$^{-1}$ mole^{-1}.

TABLE 3. *Oxidation of cyclohexanone in perchloric acid: reaction order with respect to* $[V^V]$.

[Ketone] = 0·241M, ionic strength = 2·4M.

$[V^V]$ (N)	$[H_3O^+]$ (M)	10^4k (sec.$^{-1}$)	10^4k, corr., to $[H_3O^+] = 2{\cdot}00$M
0·113	2·005	11·3	11·28
0·0565	2·061	8·75	8·48
0·0226	2·095	6·05	5·77

order reaction plots with respect to $[V^V]$ for at least 50% of the reaction. With cyclohexanone in perchloric acid, however, the velocity constant increased with $[V^V]$ as Table 3 shows. This change of reaction velocity is not due to a salt effect since the ionic strength was kept at a constant high value by the use of perchloric acid–sodium perchlorate mixtures.

(3) *Dependence of Rate on Acidity.*—In Part I the oxidising power of V^V was investigated only in aqueous sulphuric acid. Evidence of oxidation both by a univalent cation, (VO_2^+), and by another species present in stronger acid was obtained. In contrast to that of pinacol, the rate of oxidation of ketones has no acid-independent component. When perchloric acid is used solutions of V^V remain yellow from 0·1M-acidity up to the strongest solutions (*ca.* 9·5M-$HClO_4$) that were made up. Table 4 shows that for the oxidation of cyclohexanone in solutions of constant high ionic strength the rate of oxidation is of first order with respect to hydrogen-ion concentration, $[H_3O^+]$, and does not depend on the Hammett acidity function H_0.

TABLE 4. *Oxidation of cyclohexanone in perchloric acid: dependence of rate on acidity, at* 35°.

$[V^V] = 0{\cdot}056$N, [Ketone] = 0·096M, ionic strength = 6M.

$[H_3O^+]$ (M)	1·06	1·95	2·84	3·74	4·63	5·53
10^4 (sec.$^{-1}$)	2·24	4·01	5·83	7·75	9·81	12·4
H_0 (ref. 2)	−1·47	−1·83	−2·10	−2·37	−2·64	−2·93
$10^4k/[H_3O^+]$	2·11	2·06	2·05	2·07	2·12	2·14

Mean value of $k/[H_3O^+] = (2{\cdot}09 \pm 0{\cdot}03) \times 10^{-4}$ sec.$^{-1}$ mole^{-1}.

TABLE 5. *Oxidation of cyclopentanone in sulphuric acid: dependence of rate on acidity, at* 40°.

[Ketone] = 0·121M, $[V^V] = 0{\cdot}0971$N.

$[H_3O^+]$ (M)	1	2	2·87	3·81	4·75	5·18
H_0 (ref. 2)	−0·26	−0·84	−1·31	−1·77	−2·16	−2·36
$a^{\pm}$ (ref. 3)	0·1316	0·2566	0·402	0·621	0·938	1·12
10^4k (sec.$^{-1}$)	0·49	1·33	2·54	4·53	7·3	9·8

In sulphuric acid solutions, however, the rates of oxidation of both cyclopentanone and cyclohexanone increase more rapidly as the acid concentration is increased (Tables 5 and 6).

[2] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.
[3] Stokes, *Trans. Faraday Soc.*, 1948, **44**, 295.

Even in M-acid oxidation occurs in sulphuric acid about 7 times as rapidly as in perchloric acid (Table 7).

TABLE 6. *Oxidation of cyclohexanone in sulphuric acid: dependence of rate on acidity, at 25°.*

$[V^V]$ = 0·0565N, [Ketone] = 0·096M, ionic strength = 6M.

$[H_3O^+]$ (M)	1·1	3·5	5·9
10^4k (sec.$^{-1}$)	3·21	10·9	40·6
$(10^4k)^{\frac{1}{2}}/[H_3O^+]$	1·63	0·94	1·08

TABLE 7. *Comparison of oxidation rates for cyclohexanone in sulphuric and perchloric acids.*

$[V^V]$ = 0·0565N, ionic strength = 1·2M.

Temp.	[Ketone]	Acid	10^4k (sec.$^{-1}$)	10^3k/[Ketone]
35°	0·1205	H_2SO_4, 1·1M	2·43	2·02
35	0·096	$HClO_4$, 1·06M	0·301	0·314
50	0·1205	H_2SO_4, 1·1M	10·5	87·2
50	0·1205	$HClO_4$, 1·06M	1·32	11·0

(4) *Salt Effects.*—Table 8 shows that addition of sodium perchlorate markedly increases the rate of oxidation of cyclohexanone. This observation shows the importance of maintaining constant ionic strength in the measurements listed in Table 4.

TABLE 8. *Effect of sodium perchlorate on oxidation rate of cyclohexanone.*

(*a*) $[V^V]$ = 0·0565N; acid is $HClO_4$, 1·06M; [Ketone] = 0·1205M. Ionic strength adjusted with $NaClO_4$. Temp. = 50°.
(*b*) $[V^V]$ = 0·0565N; acid is H_2SO_4, 1·1M. Ionic strength adjusted with $NaClO_4$. Temp. = 25°.

	Ionic strength (M)	[Ketone]	10^4k	10^4k/[Ketone]
(*a*)	1·2		1·32	
	3·6		4·98	
	5·0		11·1	
	6·0		17·3	
(*b*)	1·2	0·116	0·87	8·5
	6·0	0·096	3·21	33·4

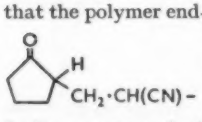
(5) *Kinetic Effects due to Transient Organic Free Radicals.*—Addition of vinyl cyanide leads to the production of insoluble polymers that contain ketonic end groups. With cyclopentanone this addition slightly increases the oxidation rate, but with cyclohexanone the oxidation rate is slightly decreased (Table 9).

TABLE 9. *Effect of addition of vinyl cyanide on oxidation rate in nitrogen atmosphere.*

(*a*) $[V^V]$ = 0·0971N; H_2SO_4, 1M; [cyclopentanone] = 0·121M. Temp. = 40°.
(*b*) $[V^V]$ = 0·0565N; $HClO_4$, 1·06M; ionic strength = 1·20M. Temp. = 50°. Ketone is cyclohexanone.
(*c*) $[V^V]$ = 0·0565N; H_2SO_4, 1·1M; ionic strength = 1·20M. Temp. = 35°. Ketone is cyclohexanone.

	[Vinyl cyanide] (M)	[Ketone] (M)	10^4k (sec.$^{-1}$)	10^3k/[Ketone]
(*a*)	0	0·121	0·313	2·59
	0·485	0·121	0·481	3·98
(*b*)	0	0·241	2·48	10·3
	0·613	0·241	1·93	8·0
(*c*)	0	0·1205	2·43	20·2
	1·20	0·1108	1·96	17·7

The infrared absorption of the polymer obtained during oxidation of cyclopentanone showed a band at 1733 cm.$^{-1}$. This indicates that the ketone was present in a five-membered ring,[4] and that the polymer end-group is as inset.



Oxygen was absorbed by oxidising solutions of both cyclopentanone and cyclohexanone. With the former, oxygen decreased the overall rate of consumption of V^V, but with the latter the effect was not so marked, indicating that the rate of destruction of the primary radical must be large compared with its rate of combination with oxygen (Table 10). V^{IV} was found to have no specific effect on the rate of oxidation of ketones.

[4] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954.

TABLE 10. *Effect of oxygen on the oxidation of ketones.*

(*a*) $[H_3O^+]$ = 1·0M (H_2SO_4); $[V^V]$ = 0·0971N; cyclopentanone used.
(*b*) $[H_3O^+]$ = 1·1M (H_2SO_4); $[V^V]$ = 0·0565N; ionic strength = 1·2M; cyclohexanone used.

	Temp.	[Ketone] (M)	Gas	10^4k (sec.$^{-1}$)
(*a*)	30°	0·121	Air	0·14
	30	0·121	N_2	0·12
	30	0·121	O_2	0·026

	Temp.	[Ketone] (M)	Gas	10^4k (sec.$^{-1}$)
(*b*)	25°	0·116	N_2, air	0·87
	25	0·116	O_2	0·96
	35	0·116	N_2	2·51
	35	0·116	O_2	2·75
	50	0·1205	N_2	10·4
	50	0·1205	O_2	9·8

(6) *Stoicheiometry of the Oxidations.*—Consecutive reactions occur in the oxidations of both ketones. With cyclopentanone and excess of V^V eventual totals of 10·3 and 10·1 equivalents of oxidant were consumed in replicate experiments. Carbon dioxide was not evolved but a test with chromotropic acid [5] indicated the production of formic acid. The conversion of cyclopentanone into an equimolar mixture of succinic and formic acids would require 10·0 equivalents of an oxidant.

Cyclohexanone, however, reduced only 6·68 and 6·14 equivalents of V^V in similar experiments, and from the reaction product adipic acid (m. p. 149°, crude; after crystallisation m. p. and mixed m. p. 152°) was isolated in 95% yield. A small amount of a brown insoluble material, not containing vanadium, was deposited as the oxidation proceeded.

2-Hydroxycyclohexanone, which was shown to be the first oxidation product when Mn^{III} was the oxidant,[6] oxidises about 200 times as fast as cyclohexanone itself, as Table 11 shows.

TABLE 11. *Comparison of oxidation rates of cyclohexanone and 2-hydroxycyclohexanone.*

$[V^V]$ = 0·0226N, $[H_3O^+]$ = 0·44M (H_2SO_4), ionic strength = 0·48M, temp. = 50°.

[Substrate]	10^4k (sec.$^{-1}$)	10^3k/[Substrate]
Cyclohexanone, 0·0125M	0·119	0·95
2-Hydroxycyclohexanone, 0·0158M	33·0	209

DISCUSSION

(1) *Nature of the Reactive Species.*—The very extensive oxidation of ketones by acid V^V is closely similar to the oxidations that can be effected by ceric and manganic salts, which also are one-electron-abstracting agents. For oxidation of cyclohexanone by manganic pyrophosphate Drummond and Waters [6] found that the limiting rate was that of the acid-catalysed enolisation of the ketone. This, at pH = 0·5 ($[H^+]$ = 0·32M, activity coefficient being assumed to be unity and sulphuric acid regarded as monobasic in this range), was $8·5 \times 10^{-3}$ mole l.$^{-1}$ hr.$^{-1}$ at 25°. Now extrapolation of Table 6 gives $5·3 \times 10^{-3}$ equiv. l.$^{-1}$ hr.$^{-1}$ for the rate of V^V oxidation of cyclohexanone at this acidity, though at a much greater ionic strength. Even at high V^V concentration no trend towards oxidation at zero-order rate in V^V has been detected (cf. Table 3). Thus in the present series of experiments it is again possible for ketone oxidation to occur subsequent to enolisation.

Under these conditions of fast enolisation and slow oxidation the acid-catalysis of the reaction must be related to the structure of the oxidant and not of the organic substrate. Now, quinquevalent vanadium is completely converted into a univalent cation, VO_2^+, even in 0·1M-mineral acid, but the oxidations of the two ketones are wholly acid-dependent (Tables 4, 5, 6) so that, in contrast to the case of pinacol, the cation VO_2^+ cannot be an active oxidant. The occurrence at higher acidities of the rapid equilibrium $H_3O^+ + VO_2^+ \rightleftharpoons V(OH)_3^{2+}$ can be postulated,[7] and if $V(OH)_3^{2+}$ is presumed to be an active oxidant this equilibrium would account for the observations made in perchloric acid, where the acid-dependence is on $[H_3O^+]$ and not on Hammett's h_0, as would probably be the case with a cation $VO{\cdot}OH^{2+}$ that did not incorporate a water molecule.

The marked positive salt effect again indicates that the rate-determining reaction involves a charged ion, whilst colorimetric measurements fail to yield confirmatory evidence

[5] Feigl, "Spot Tests," Elsevier, Amsterdam, 1947.
[6] Drummond and Waters, *J.*, 1955, 497.
[7] Ramsey, Colichman, and Pack, *J. Amer. Chem. Soc.*, 1946, **68**, 1695; Boyer and Ramsey, *ibid.*, 1953, **75**, 3802.

of the presence of two different ions, VO_2^+ and $V(OH)_3^{2+}$, in perchloric acid solutions of V^V. The noticeable colour change from yellow to red in sulphuric acid solutions, together with the kinetic measurements of Tables 4—7, establishes without doubt the existence of a charged sulphate complex, such as $V(O{\cdot}SO_3H)_3^{2+}$ or $VO(O{\cdot}SO_3H)^{2+}$ or $V(OH)_3HSO_4^+$ of enhanced oxidising power. The last would give second-order dependence on sulphuric acid as approximately indicated by Table 6. Complex formation of this type accords, too, with the fact (Table 8) that the salt effect is somewhat less in sulphuric than in perchloric acid. Again, the solubility of V^V in sulphuric acid is much greater than in perchloric acid; 0·4N-solutions of V^V in 4M-sulphuric acid are quite stable and vanadium pentoxide dissolves easily in concentrated sulphuric acid, while 0·2N-solutions of V^V in 4·4M-perchloric acid precipitate vanadium pentoxide when warmed above 60°, and only 0·02N-solutions of V^V can be prepared at room temperature in 60% perchloric acid by direct dissolution of vanadium pentoxide in the acid. Light absorption of V^V solutions in sulphuric acid is noticeably shifted towards longer wavelengths than that of solutions in perchloric acid but, since in both solvents the absorption maximum occurred below 2000 Å, spectrophotometric measurements could not be used to investigate the extent of sulphuric acid complex formation.

(2) *Mechanism of Ketone Oxidation.*—The effects of adding vinyl cyanide and oxygen to both reacting ketones show conclusively that free organic radicals must be formed,[1] and thus V^V cannot be reduced below the valency level V^{IV}. The strict first-order dependence of the oxidation rate on ketone concentration indicates that complex formation does not occur noticeably before the oxidation step (compare oxidations of 1,2-diols and of pyruvic acid by manganic pyrophosphate[6,8]). Comparison with the conclusions of Drummond and Waters concerning cyclohexanone oxidation by manganic pyrophosphate is of interest: $V(OH)_3^{2+}$ is the slower oxidant of cyclohexanone but it is a much faster oxidant of 2-hydroxycyclohexanone. The ultimate degradation of the ketones, however, does not differ significantly from that found with any other one-electron-abstracting agents.

Experimental

Materials.—V^V *Solutions.* " AnalaR " ammonium metavanadate was dissolved or suspended in distilled water, and the calculated quantity of acid added. When solutions in perchloric acid (B.D.H.) were required it was essential that all the vanadate should be in solution, to minimise or eliminate precipitation of vanadium pentoxide. The acidity was determined and the ionic strength adjusted before the acid was added to the ammonium vandate solution, as addition of ammonium vanadate does not affect the ionic strength of the acid solution used:

$$2H^+ + NH_4VO_3 \rightleftharpoons VO_2^+ + NH_4^+ + H_2O$$

The $[V^V]$ was then found by titration, and a corrected acidity value was calculated from the above equation. The ionic strength was adjusted by using sodium perchlorate (Hopkin and Williams's " recrystallised " grade) which was shown not to contain sufficient chlorate to interfere with the titration of Fe^{2+} by V^V. Solutions of this were standardised by weighing the sodium perchlorate remaining after evaporation to dryness and ignition to 160°, at which temperature the anhydrous salt is stable.[9]

Cyclopentanone was purified *via* its bisulphite compound, which was decomposed with acid, and the ketone extracted with ether. The ether was distilled off, and the fraction, b. p. 128—130°, was collected and refractionated. The purity was checked by the infrared spectrum.[10]

Cyclohexanone was purified by the bisulphite compound, which was decomposed with sodium carbonate,[11] the ketone steam-distilled off, and the dry, washed, ethereal extract was carefully fractionated under nitrogen.

[8] Drummond and Waters, *J.*, 1953, 3119.
[9] Duval, *Analyt. Chim. Acta*, 1947, **1**, 341.
[10] Randall, Fowler, Fuson, and Dangl, " Infrared Determination of Organic Structures," D. Van Nostrand Co. Inc., 1949.
[11] Garland and Reid, *J. Amer. Chem. Soc.*, 1925, **47**, 2333.

Pure 2-hydroxycyclohexanone was kindly given by Dr. M. L. Tomlinson.

Kinetic Measurements.—These were carried out as in Part I, except that for the work at 50° a totally enclosed reaction vessel, having two bulbs in which the unmixed reactants could be allowed to reach the temperature of the thermostat, was used. At zero time one bulb was rotated at a ground-glass joint, and the liquids were mixed by manual shaking. The whole vessel, except for a stoppered neck through which samples could be withdrawn, was immersed below the surface of the thermostat liquid.

It has been found that, in the absence of daylight, accurate titrations, by the procedure described in Part I, can be carried out in diffused light from a mercury lamp, filtered through glass.

One of us (J. S. L.) thanks the Salters' Company for a scholarship, during the tenure of which part of this work was carried out.

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, January 13th*, 1959.]

---

604. *The Kinetics of Diazo-coupling and Iodination of Glyoxaline and Some Deuteroglyoxalines.*

By A. GRIMISON and J. H. RIDD.

Diazo-coupling of glyoxaline and of 2,4,5-trideuteroglyoxaline occur at about the same rate, but in iodination of these two compounds the $k_H : k_D$-ratio is about 4·5. The iodination is catalysed by glyoxaline and anti-catalysed by iodide ions, but changes in the concentrations of these species have little effect on the $k_H : k_D$ ratio. The relative rates of iodination of 2-deutero-, 4,5-dideutero-, and 2,4,5-trideutero-glyoxaline show that the initial substitution occurs at the 4(5)-position. The mechanism of iodination is discussed in relation to recent studies of the iodination of phenol.

KINETIC studies of the diazo-coupling [1] and iodination [2] of glyoxaline have already been reported, and this work has now been extended to the deuteroglyoxalines. The preparation of 2-deutero-, 4,5-dideutero-, and 2,4,5-trideutero-glyoxaline has recently been described.[3] Analytical figures for deuterium and the proton magnetic resonance spectra of the samples used in these kinetic studies show almost complete deuteration at the stated positions. From related experiments on the deuteration of glyoxaline, it can be calculated that the exchange of deuterium between glyoxaline and the media used for diazo-coupling and iodination is negligible during a kinetic run. The full kinetic isotope effect in these substitution reactions should therefore be observed.

Deuterium-substitution at carbon atoms is known to affect acid–base equilibria at adjacent oxygen or nitrogen atoms.[4] Two such equilibria are important in the diazo-coupling and iodination reported here. The reactions are believed to involve the conjugate base of glyoxaline, and so the acidity of glyoxaline (GH) determines the concentration of the reactive form of glyoxaline (G^-) present in the solution. The basicity of glyoxaline determines the pH of the medium, for, in this work, the equilibrium $GH_2^+ \rightleftharpoons GH + H^+$ was used to buffer the solutions. The effect of deuterium substitution on the equilibrium was carefully investigated but any difference in the basicity of glyoxaline and 2,4,5-trideuteroglyoxaline is less than 0·01 pK unit, and, for our purposes, can be ignored. The same is presumably true of the acidity of the two molecules involved.

Diazo-coupling.—The reaction was carried out in aqueous solution in the presence of a large excess of glyoxaline partly neutralised with perchloric acid. Since these solutions

[1] Brown, Duffin, Maynard, and Ridd, *J.*, 1953, 3937.
[2] Ridd, *J.*, 1955, 1238.
[3] Gillespie, Grimison, Ridd, and White, *J.*, 1958, 3228.
[4] Halevi, *Tetrahedron*, 1957, **1**, 174.

were more acidic than those studied previously, and also contained a far higher concentration of glyoxaline, the kinetic form of the reaction was briefly redetermined. It seemed possible that a base-catalysed term was present in the coupling mechanism, analogous to that found in the presence of similar concentrations of glyoxaline in the kinetics of iodination.

Experiments with different initial concentrations of diazonium ions showed that the reaction was of the first-order with respect to diazonium ions and, where side-reactions could be ignored, the formation of the azo-glyoxaline followed a first-order law during a single kinetic run. Details of some kinetic runs carried out to determine the order with respect to glyoxaline and hydrogen ions are given in Table 1. The third and the fourth column indicate the initial concentrations of glyoxaline (GH) and the glyoxalinium ion (GH_2^+); these determine the hydrogen-ion concentration, and the calculated values of this are given in column 5, the dissociation constant of the glyoxalinium ion being taken as 10^{-7}. The first-order rate coefficient (k_1) is given in column 6, followed by the second-order rate coefficient (k_2) obtained by dividing k_1 by the concentration of unprotonated glyoxaline in the solution. The third-order rate coefficient (k_3) in the last column is obtained by multiplying k_2 by the hydrogen-ion concentration in the solution. The

TABLE 1. *Rate coefficients for the reaction between glyoxaline and diazotised sulphanilic acid.**

Temp.	Ionic strength	[GH] †	$[GH_2^+]$	$10^7[H^+]$	10^4k_1 ($sec.^{-1}$)	10^3k_2 ($sec.^{-1}$ $mole^{-1}$ l.)	10^9k_3 ($sec.^{-1}$)
25°	0·030	0·030	0·030	1·00	12 ‡	4·0	4·0
25	0·030	0·020	0·020	1·00	7·3 ‡	3·6	3·6
25	0·030	0·010	0·010	1·00	3·6 ‡	3·6	3·6
0	0·052	0·033	0·027	0·82	5·5	1·67	1·37
0	0·052	0·043	0·017	0·395	13·8	3·21	1·27
0	0·052	0·073	0·047	0·64	15·4	2·11	1·35

* The concentration of diazonium ions was 5×10^{-5}M for the first three runs and 5×10^{-3}M for the remainder.

† In the work already reported [1, 2] the symbol [GH] is used in the Tables for the stoicheiometric concentration of glyoxaline; here it is used for the concentration of unprotonated glyoxaline in the solution. The latter usage conforms to that in the kinetic equations.

‡ Based on initial rates; see Experimental section.

constancy of k_3 at a given temperature indicates that k_1 is proportional to the glyoxaline concentration and inversely proportional to the hydrogen-ion concentration. The kinetic form therefore fits equation (1), in agreement with the earlier kinetic study. In particular, the first three runs in Table 1 show that there is no significant evidence of base catalysis when the pH is maintained constant.

$$\text{Rate} = k_3[GH][ArN_2^+]/[H^+] = k'[G^-][ArN_2^+] \quad . \quad . \quad . \quad . \quad (1)$$

The diazo-coupling of glyoxaline was then compared with that of 2,4,5-trideuteroglyoxaline. The spectrum of the solutions after reaction agreed with that of the 2-azo-compound apart from a small discrepancy at about 2500 Å, and the calculated concentration

TABLE 2. *Comparison of the coupling of glyoxaline and 2,4,5-trideuteroglyoxaline with diazotised sulphanilic acid at 25°.*

[GH] = 0·033M. $[GH_2^+]$ = 0·027M. $10^7[H^+]$ = 0·82M. $[ArN_2^+]$ = 0·005M.

Time (min.)	Reaction (%) $C_3H_4N_2$	Reaction (%) $C_3D_3HN_2$	Time (min.)	Reaction (%) $C_3H_4N_2$	Reaction (%) $C_3D_3HN_2$
0·0	11	9	2·0	32	30·5
0·5	18	15	2·5	36	35
1·0	23	21	3·0	40	39
1·5	29	27	3·5	43	43

of azo-compound corresponded to about 80% reaction. The details of two of the kinetic runs are given in Table 2; the difference between the initial reaction rates is almost within

the experimental error, but it may be significant because, in other pairs of runs, the deutero-compound was always the slower. However, it is clear that there is no major isotope effect in the reaction.

Iodination.—It has been shown previously [2] that the kinetics of iodination of glyoxaline by molecular iodine in an aqueous solution of potassium iodide follow equation (2); this is equivalent to equation (3) when the equilibria in the solution are taken into account. The reaction path corresponding to the first term in these equations will be referred to as the uncatalysed reaction, and that corresponding to the second as the self-catalysed reaction:

$$\text{Rate} = k\frac{[\text{GH}][\text{I}_3^-]}{[\text{H}^+][\text{I}^-]^2} + k_{\text{cat}}\frac{[\text{GH}]^2[\text{I}_3^-]}{[\text{H}^+][\text{I}^-]^2} \quad . \quad . \quad . \quad . \quad (2)$$

$$\text{Rate} = k'[\text{G}^-][\text{I}^+] + k'_{\text{cat}}[\text{G}^-][\text{I}^+][\text{GH}] \quad . \quad . \quad . \quad . \quad (3)$$

The kinetics of iodination of 2,4,5-trideuteroglyoxaline were studied under the same conditions but by a spectrophotometric method instead of by the titration of samples with sodium thiosulphate. The concentrations of glyoxaline (partly neutralised with perchloric acid) and of iodide ions were sufficiently large to remain effectively constant

TABLE 3. *Comparison of the iodination of glyoxaline and 2,4,5-trideuteroglyoxaline at 25°.*

$[\text{H}^+] = 10^{-7}$M. $[\text{I}^-] = 0{\cdot}01$M. $[\text{I}_2] = 0{\cdot}001$M. Ionic strength = 0·05.

	10^4k_1 (sec.$^{-1}$)		10^2k_2 (sec.$^{-1}$ mole^{-1} l.)	
$[\text{GH}]^* = [\text{GH}_2^+]$	$C_3H_4N_2$	$C_3HN_2D_3$	$C_3H_4N_2$	$C_3HN_2D_3$
0·04	18·8	4·18	4·7	1·05
0·025	9·38	1·89	3·36	0·757
0·015	3·84	0·865	2·56	0·576
0·0075	1·29	0·317	1·72	0·422

* See footnote † to Table 1.

throughout a single kinetic run; the only variable was then the concentration of molecular iodine (present in the solution as I_3^- ions). Excellent first-order kinetics were observed and a set of first-order rate coefficients is compared in Table 3 with those obtained in the same way for the iodination of glyoxaline. From a comparison of the two sets of first-order rate coefficients, it is clear that a major isotope effect is present in the reaction.

These results enable $k_H : k_D$ ratio to be evaluated for both the uncatalysed and the self-catalysed reactions. Second-order rate-coefficients (k_2) obtained by dividing the first-order rate coefficients (k_1) by the concentration of unprotonated glyoxaline or trideuteroglyoxaline are also listed in Table 3. The values of k_2 increase linearly with the substrate concentration because of the self-catalysed term in the kinetic equation. In Fig. 1, the k_2 values are plotted against the substrate concentration (glyoxaline or trideuteroglyoxaline). The relative intercept of the graphs on the vertical axis give the $k_H : k_D$ ratio for the uncatalysed reaction, and the relative slopes of the graphs give the $k_H : k_D$ ratio for the catalysed reaction. Since both graphs can be projected to pass through almost the same point on the axis of abscissæ, it is clear that the kinetic isotope effect is very similar for the two reaction paths. Calculation gives $k_H : k_D = 4{\cdot}36$ for the uncatalysed reaction and $k_H : k_D = 4{\cdot}47$ for the self-catalysed reaction.

The concentration of iodide ions in the above kinetic runs was 0·01M. Some experiments were carried out in the absence of potassium iodide, with 50% (v/v) aqueous methanol as the reaction medium. The kinetic form of the reaction under these conditions was not investigated in detail, but the results showed that the kinetic isotope effect was almost unchanged. The variation of the optical density of the solutions arising from absorption by molecular iodine in the reaction of glyoxaline and 2,4,5-trideuteroglyoxaline under equivalent conditions is shown in Fig. 2; the initial reaction rates vary by about a factor of 4. The maximum concentration of iodide ions arising from the iodination, illustrated

in Fig. 2, cannot exceed 0·0005M. The significance of these results is discussed below with reference to recent studies on the iodination of phenol.

The iodination of glyoxaline under the conditions set out in Table 3 leads mainly to 2,4-di-iodoglyoxaline.[2] The kinetic form of the substitution, and the formation of the di-iodo-product in the presence of excess of glyoxaline, show that introduction of the first iodine atom must be the rate-determining stage. The presence of an isotope effect in the iodination makes it possible to determine the initial position of substitution. The rates

TABLE 4. *Variation of the kinetic isotope effect (at 25°) with the position of deuteration.*

[GH] = [GH_2^+] = 0·04M. [H^+] = 10^{-2}M. [I^-] = 0·01M. [I_2] = 0·001M.

	Glyoxaline	2,4,5-Trideutero-	4,5-Dideutero-	2-Deutero-
10^4k_1 (sec.$^{-1}$)	18·8	4·18	5·05	14·9
k_1^H/k_1^D	—	4·5	3·7	1·26

of iodination of glyoxaline and a group of deuteroglyoxalines are shown in Table 4; the large isotope effect observed with the trideutero-compound is mainly present in the

FIG. 1. *Variation of second-order rate coefficient in iodination with substrate concentration*: (○) *glyoxaline*; (●) *2,4,5-trideuteroglyoxaline.*

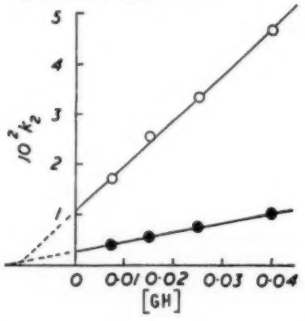
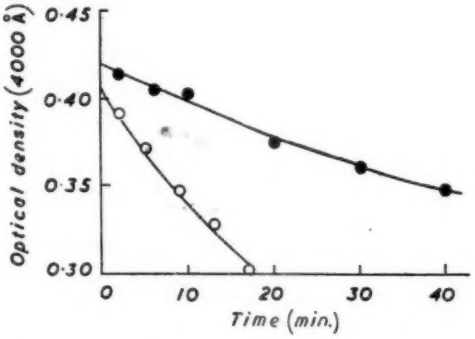


FIG. 2. *Iodination in 50% (v/v) aqueous methanol at 25°; [GH] = 0·005M, [GH_2^+] = 0·025M; [I_2] = 0·0005M; (○) glyoxaline; (●) 2,4,5-trideuteroglyoxaline.*



iodination of 4,5-dideuteroglyoxaline, but almost absent in the iodination of 2-deuteroglyoxaline. This indicates that the C–H bond at the 4(5)-position is weakened in the rate-determining step, and therefore implies that, under these conditions, the initial substitution is mainly at the 4(5)-position.

The initial substitution has been previously considered to occur at the 2-position, although the evidence for this has never been conclusive and has relied mainly on the isolation of a small amount of the 2-iodo-compound under conditions where the greater part of the iodine is finally present as di- and tri-iodo-compounds.[5] This early work was carried out under strongly alkaline conditions, and a change in the pH of the medium may itself alter the orientation; this point is being investigated further. The fact that at pH 7 iodination leads to attack at the 4(5)-position while diazo-coupling leads to attack at the 2-position, is not fully understood; a possible interpretation has been given elsewhere.[6]

Comparison with Substitution in Phenol.—The above results indicate a significant correspondence between the substitution reactions of glyoxaline and of phenol. The kinetic equations for the diazo-coupling of the two substrates have the same form,[7] and those for iodination differ only in the second term.[8] In the iodination of phenol, the

[5] Pauly and Arauner, *J. prakt. Chem.*, 1928, **118**, 33.
[6] Grimison and Ridd, *Proc. Chem. Soc.*, 1958, 256.
[7] Zollinger, *Chem. Rev.*, 1952, **51**, 347.
[8] Berliner, *J. Amer. Chem. Soc.*, 1951, **73**, 4307.

second term includes a molecule of the buffer; in the iodination of glyoxaline, the second term includes an extra molecule of glyoxaline. This difference can be explained because, in the latter reaction, the concentration of glyoxaline is sufficient for glyoxaline to act as both the substrate and the buffer.[2]

The similarity in the kinetic equations extends also to the kinetic isotope effects. In the diazo-coupling of phenol,[9] as in that of glyoxaline, the $k_H : k_D$ ratio is almost unity. In the iodination of phenol the $k_H : k_D$ ratio has been recently reported [10] to be 3·97; in comparison, the value here reported for the iodination of 2,4,5-trideuteroglyoxaline is 4·5. No evidence on the variation of the $k_H : k_D$ ratio in the iodination of phenol has yet been published.

It is generally agreed that diazo-coupling and iodination of phenol involve substitution of the phenoxide ion, and the above correspondence of the kinetic equations makes it very probable that the same substitutions in glyoxaline also involve the conjugate base of the substrate. The correspondence of the kinetic isotope effects suggests that the transition state for substitution at a carbon atom in the conjugate base of glyoxaline is similar to that for substitution in the phenoxide ion.

As a result of this correspondence, the details of this kinetic study have a bearing on the mechanism of aromatic iodination. There has recently been some discussion [10,11] as to whether the kinetic equation for iodination, illustrated for glyoxaline by equations (2) and (3), results from the attack of I^+ or of H_2OI^+ on the substrate (SH) or involves the reversible formation of an intermediate (SHI^+) by the reaction $SH + I_2 = SHI^+ + I^-$. The intermediate could either lose an I^+ ion by the reverse reaction above, or lose a proton by reaction with some Brönsted base in the solution. If the reaction with iodide ions occurred more readily than that with a Brönsted base, then the proton-loss would be effectively rate-determining, and the kinetic isotope effect would be explained. However, it is then a little surprising that the $k_H : k_D$ ratio should be almost unchanged when the concentration of iodide ions at the start of the reaction is decreased from 0·01M to zero (compare the results in Figs. 1 and 2). This suggests that the isotope effect does not depend on the rapid back-reaction of any intermediate with iodide ions, although it is difficult to be certain that a minute iodide-ion concentration does not compete effectively with the reaction involving proton loss.

A further problem concerns the rôle of the base in the second term of the kinetic equation. From the results in Fig. 1 it can be seen that the $k_H : k_D$ ratio for the self-catalysed reaction is independent of the glyoxaline concentration and almost equal to the $k_H : k_D$ ratio for the uncatalysed reaction. These results are a little more consistent with the idea that the base catalyses the reactions mainly by the formation of an alternative iodinating agent rather than by participating directly in the loss of the proton. In the related iodinations of aniline derivatives the buffer-catalysis remains effective when there is no kinetic isotope effect; [12] this shows clearly that a mechanism of buffer catalysis other than by proton removal is available.

Experimental

Materials.—The glyoxaline was purified by recrystallisation and sublimation; almost all the other reagents were of "AnalaR" quality. The deuteroglyoxalines were prepared as described previously.[3] Hydrogen–deuterium analyses were as follows: 2,4,5-trideuteroglyoxaline, 75% D; 4,5-dideuteroglyoxaline 50·2% D; 2-deuteroglyoxaline, 24·5% D. Slight deuteration at unstated positions may be present in the last two compounds. The basicity measurements were carried out by taking a large number of pH readings on partly neutralised solutions of glyoxaline, a Cambridge pH meter being used in a room maintained at a constant

[9] Zollinger, personal communication of preliminary experiments.
[10] Grovenstein and Kilby, *J. Amer. Chem. Soc.*, 1957, **79**, 2972.
[11] Grovenstein and Henderson, *ibid.*, 1956, **78**, 569.
[12] Shilov and Weinstein, *Nature*, 1958, **182**, 1300.

XUM

temperature. Details are available elsewhere.[13] The azo-compound from diazotised sulphanilic acid and glyoxaline was prepared by conventional methods (Found: C, 42·0; H, 3·9; N, 22·5. Calc. for $C_9H_8O_3N_4S$: C, 42·9; H, 3·2; N, 22·2%). The absorption spectrum above 2400 Å in water consists of a single peak of $\lambda_{max.}$ 3660 Å (ε $2·2 \times 10^4$); in 0·1N-aqueous perchloric acid, this is changed to $\lambda_{max.}$ 3550 Å (ε $2·42 \times 10^4$).

Kinetic Studies of Diazo-coupling.—The kinetic runs with an initial diazonium ion concentration of 5×10^{-5}M were carried out in an optical cell maintained at 25° in a Unicam S.P. 500 spectrophotometer, and were followed from the increase in the optical density at 3660 Å arising from absorption by the 2-azoglyoxaline formed. Kinetic runs involving greater initial concentrations of diazonium ions were followed by extracting samples and running these into 0·1M-aqueous perchloric acid. This stopped the reaction, and the spectrum of the solution was

TABLE 5. *Details of one of the kinetic runs given in Table* 3.

[GH] = 0·04M. $[GH_2^+]$ = 0·04M. $[I^-]$ = 0·01M. $[I_2]$ = 0·001M.

Time (min.)	Optical density at 4400 Å	log (O.D. × 10)	10^4k_1 (sec.$^{-1}$)	Time (min.)	Optical density at 4400 Å	log (O.D. × 10)	10^4k_1 (sec.$^{-1}$)
0	0·520	0·716	—	10	0·169	0·228	18·8
2	0·414	0·617	19·1	12	0·134	0·127	18·9
4	0·332	0·521	18·7	14	0·105	0·021	19·1
6	0·263	0·420	19·0				
8	0·211	0·324	18·8				

then compared with that of solutions of the 2-azo-compound. The faster kinetic runs at 0° led to more than 95% of azo-coupling, but at 25° some side-reaction, presumably the decomposition of the diazonium ion, decreased the yield of azo-compound. The first-order rate coefficients were then calculated from the initial rates. Within each group of runs the ionic strength was brought to a constant value by the addition, where necessary, of sodium perchlorate.

Kinetic Studies of Iodination.—Most of the kinetic runs were carried out by adding a solution of iodine in aqueous potassium iodide at 25° to a partly neutralised solution of glyoxaline in an optical cell maintained at 25° by a thermostat. The ionic strength of the final solution was brought to 0·05 by the presence, where necessary, of sodium perchlorate. Details of a typical kinetic run are given in Table 5. For the kinetic runs illustrated in Fig. 2, this procedure was modified by dissolving the iodine in methanol and by having some methanol present in the glyoxaline solution. The extent of the reaction was determined from the absorption due to molecular iodine and tri-iodide ions at 4400 Å, a Unicam S.P. 500 spectrophotometer being used. The rate constants so calculated agreed excellently with those obtained by extracting samples and titrating the unchanged iodine with sodium thiosulphate. A product analysis carried out under conditions similar to those in the kinetic runs gave 2,4-di-iodoglyoxaline in 67% yield; no other products could be detected.

The authors thank Professor E. D. Hughes, F.R.S., and Sir Christopher Ingold, F.R.S., for their interest in this work, and Mr. T. A. Claxton for assistance in some of the experiments.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER STREET,
LONDON, W.C.1.

[*Received, February 4th*, 1959.]

[13] Grimison, Ph.D. Thesis, London, 1958.

605. *Polycyclic Cinnoline Derivatives. Part II.* The Symmetrical Dinaphthopyridazines.*

By R. S. W. Braithwaite and P. F. Holt.

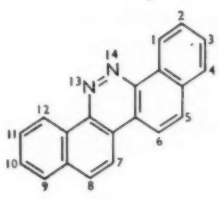
Benzo[*h*]naphtho[1,2-*c*]cinnoline, benzo[*f*]naphtho[2,1-*c*]cinnoline, and 1,2,3,4,9,10,11,12-octahydrobenzo[*g*]naphtho[2,3-*c*]cinnoline have been prepared by reducing dinitrobiaryls. An approach to the chemistry of these cinnolines has been made, in particular, a study of the nitration products of the first two. The product of reduction of 10,10′-dinitro-9,9′-biphenanthryl differs from a substance reported to be dibenzo[*f*,*h*]phenanthro[9,10-*c*]-cinnoline.

Polycyclic cinnoline systems of more than three rings appear not to have been studied systematically, and indeed very few such systems appear to be known. Benzo[*f*]naphtho-[2,1-*c*]cinnoline (III) and its *N*-oxide were prepared [1] incidentally to a study of the reduction of 2-nitronaphthalene, and dibenzo[*f*,*h*]phenanthro[9,10-*c*]cinnoline (IV) was produced by Schönberg and Rosenthal [2] by subliming an epoxide which Zincke [3] had found as an unidentifiable product in the reaction between phenanthraquinone imine and acetic anhydride.

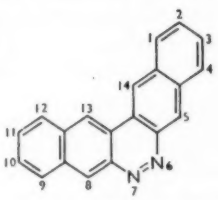
Some of the polycyclic cinnolines are analogues of the carcinogenic hydrocarbons and those in which the azo-group replaces the carbon atoms of the *K*-region would be of particular interest, as the azo-group would increase the electron-density of this region. The theory which relates the electron density of the *K*-region to the carcinogenicity of the compound (see, for example, Schmidt [4]) suggests that these cinnoline analogues will have a very high carcinogenic activity.

One general method which has been applied to the production of the simpler benzo[*c*]-cinnolines involves the formation and subsequent reduction of 2,2′-dinitrobiaryls, and a study of this method has been reported by Braithwaite, Holt, and Hughes.[5] This method has now been applied to the synthesis of higher cinnolines.

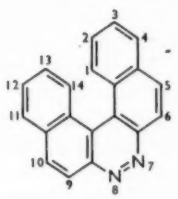
An attempt was first made to synthesise and to study the properties of members of the ring systems of the three possible symmetrical dinaphthopyridazines (I)—(III), and the diphenanthropyridazine (IV). As the direct synthesis of benzo[*g*]naphtho[2,3-*c*]cinnoline



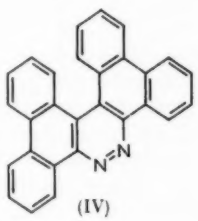
(I)



(II)



(III)



(IV)

(II) requires 2-halogeno-3-nitronaphthalenes as starting materials, which have been prepared only in very small quantities (*e.g.*, by Hodgson and Elliott [6]), the more readily available 1,2,3,4-tetrahydro-6-iodo-7-nitronaphthalene was used to prepare a hydrogenated derivative of (II).

* Part I, *J.*, 1948, 4073.

[1] Meisenheimer and Witte, *Ber.*, 1903, **36**, 4153.
[2] Schönberg and Rosenthal, *Ber.*, 1921, **54**, 1789.
[3] Zincke, *Ber.*, 1879, **12**, 1641.
[4] Schmidt, *Naturwiss.*, 1941, **29**, 146.
[5] Braithwaite, Holt, and Hughes, *J.*, 1958, 4073.
[6] Hodgson and Elliott, *J.*, 1936, 1151.

The obvious route to the more complex dinitrobiaryls is by the Ullmann reaction, but yields are often very low. Dimethylformamide has been found to increase the yield of dinitrobinaphthyl from 1-iodo-2- and 2-iodo-1-nitronaphthalene to 80%, apparently owing to the solvent action of the dimethylformamide in which the copper halide, the reactant, and the products dissolve leaving the copper surface uncoated.

The yields of biaryls from 4-bromo-1-iodo-2-nitronaphthalene and 1,2,3,4-tetrahydro-6-iodo-7-nitronaphthalene are, however, not improved by dimethylformamide, and the solvent causes halogen to be eliminated without biaryl formation when 9-bromo-10-nitrophenanthrene and 1-chloro-2,6-dinitrobenzene react with copper. In the latter case the absence of biaryl formation is presumably due to steric hindrance, but this cannot apply to the phenanthrene derivative because 1-iodo-2-nitronaphthalene, in which the groups have similar spatial relations, gives a high yield of biaryl. The partly aliphatic nature of the 9,10-bond of phenanthrene is probably relevant; vinyl halides do not undergo the Ullmann reaction.

The dinitrobiaryls were reduced by one or more of the reagents, lithium aluminium hydride, sodium amalgam and methanol, sodium sulphide, and zinc and potassium hydroxide. Conforming to the generalisations made earlier (Braithwaite, Holt, and Hughes [5]) these always gave cinnolines or their oxides, except that sodium amalgam and methanol produced diamines from 2,2′-dinitro-1,1′- and 1,1′-dinitro-2,2′-binaphthyl (confirming the observation by Chudožilov [7]), and zinc and potassium hydroxide produced a dehalogenated cinnoline from 4,4′-dibromo-2,2′-dinitro-1,1′-binaphthyl.

On reduction with lithium aluminium hydride, 10,10′-dinitro-9,9′-biphenanthryl gave a substance (m. p. >360°) that was not identical with the cinnoline (m. p. 290°) assumed to be (IV) by Schönberg and Rosenthal.[2] The yield was so small that a full investigation and analysis was impossible but the new substance appeared to be a cinnoline.

Although 1,1′-dinitro-2,2′-binaphthyl gave benzo[*h*]naphtho[1,2-*c*]cinnoline (I) with lithium aluminium hydride at room temperature, under reflux a dihydrocinnoline was formed which was also formed directly from the cinnoline by a similar reduction process. The dihydro-compound had the yellow colour which is characteristic of cinnolines, formed a red hydrochloride more stable than the hydrochloride of (I), and was readily oxidised by air. It formed a coloured solution in concentrated sulphuric acid, as do all cinnolines. These properties indicate that the new compound contains an unreduced cinnoline ring system. Bohlmann [8] detected a reduction product assumed to be the *NN*′-dihydro-derivative when he treated benzo[*c*]cinnoline with lithium aluminium hydride, though he found the substance too unstable for isolation. In picene, the homocyclic analogue of (I), the 5,6-bond is most easily attacked. By analogy, the new compound appears to be 5,6-dihydrobenzo[*h*]naphtho[1,2-*c*]cinnoline.

Benzo[*h*]naphtho[1,2-*c*]cinnoline *N*-oxide, prepared by reducing 1,1′-dinitro-2,2′-binaphthyl with sodium sulphide, and by oxidation of the cinnoline by hydrogen peroxide, appears to be identical with a substance reported by Cumming and Howie [9] as 1-amino-1′-nitro-2,2′-binaphthyl. Similarly, the compound reported by Cumming and Howie [9] to be 2-amino-2′-nitro-1,1′-binaphthyl appears to be identical with benzo[*f*]naphtho[2,1-*c*]-cinnoline *N*-oxide, previously prepared by Meisenheimer and Witte,[1] the constitution of which we have proved from its oxygen content and its formation by oxidation of the cinnoline. Cumming and Howie gave N = 9·3%. The calculated value for the amino-nitrobiaryl is 8·9% and for the cinnoline *N*-oxide, 9·4%.

Little of the chemistry of the polycyclic cinnolines has been described. Of the simple derivatives, picrates have been derived from two such cinnolines.[2,10,11] We have produced

[7] Chudožilov, *Chem. Listy*, 1925, **19**, 187.
[8] Bohlmann, *Ber.*, 1952, **85**, 390.
[9] Cumming and Howie, *J.*, 1932, 528.
[10] Sandin and Cairns, *J. Amer. Chem. Soc.*, 1936, **58**, 2019.
[11] Slack and Slack, *Nature*, 1947, **160**, 437.

a monopicrate from compound (III) and a hemipicrate from compound (I), but have not succeeded in producing addition products with 1,3,5-trinitrobenzene from the latter base.

Benzo[*c*]cinnoline is known to form a methiodide and an ethiodide [12] from which the tertiary base is regenerated by ammonia.[13] We find that a methotri-iodide is given when our base (III) is treated with methyl iodide. Since ammonia or sodium carbonate regenerates the original base, and no iodine is produced when the tri-iodide is heated, nuclear substitution by iodine and adsorption of free iodine are both excluded: the salt must contain the tri-iodide ion. Wohlfahrt [12] reported that benzo[*c*]cinnoline methiodide combined with iodine when shaken with ethanolic iodine. No quaternary compound could be isolated from a mixture of compound (I) with methyl iodide; a transitory colour change suggested that a methiodide may be formed but that it is too unstable to be separated.

Different cinnolines vary in their reaction to reducing agents. Benzo[*c*]cinnoline is unaffected by sodium amalgam in methanol but it gives an unstable dihydro-derivative with zinc dust and either hydrochloric acid [14] or potassium hydroxide,[15] and with lithium aluminium hydride.[8] A dihydro-derivative is also formed when compound (III) is reduced with stannous chloride.[1] The compound (III) is reduced to the diaminobinaphthyl [1] by zinc and acetic acid, but the heptacyclic analogue (IV) is unaffected.[2]

We find that both benzonaphthocinnolines (I) and (III) give good yields of the diaminobinaphthyls with sodium amalgam, and that the former gives the corresponding carbazole with zinc and acetic acid and a dihydro-derivative with lithium aluminium hydride.

Benzo[*c*]cinnoline *N*-oxide and its derivatives have been reduced by stannous chloride to the corresponding cinnolines.[13,16-18] The *N*-oxide of compound (I) gave the parent cinnoline with stannous chloride, and that of its analogue (III) a colourless solution probably of the dihydro-derivative, which gave the parent base (III) in good yield on addition of alkali. It appears that cinnoline oxides generally are reduced to cinnolines or their unstable dihydro-derivatives by stannous chloride.

Lithium aluminium hydride, with which Badger, Seidler, and Thomson [19] reduced benzo[*c*]cinnoline *N*-oxide to the cinnoline, also reduces the *N*-oxides of our compounds (I) and (III) to the cinnolines. Coloured intermediates are formed similar to those observed in the reduction of the corresponding dinitrobinaphthyls.

The only reports on the oxidation of polycyclic cinnolines appear to be those of Taüber [20] who obtained pyridazine-1,2,3,4-tetracarboxylic acid by treating benzo[*c*]-cinnoline with alkaline permanganate, and Schönberg and Rosenthal [2] who observed that compound (IV) is unaffected by alkaline permanganate but obtained phenanthraquinone with chromium trioxide. We found that peracetic acid converts benzo[*c*]cinnoline and compounds (I) and (III) into the cinnoline *N*-oxides. Alkaline permanganate and chromium trioxide in acetic acid do not affect either of the last two bases, the rings adjacent to the pyridazine ring being protected by the additional rings.

The only reports of the nitration of a polycyclic cinnoline refer to benzo[*c*]cinnoline and its *N*-oxide. After several days a concentrated solution of compound (III) in fuming nitric acid at room temperature yields two isomeric dinitro-derivatives. The compound (I) also yields a dinitro-derivative when nitrated by a similar method. The determination of the orientation of these dinitro-compounds will be difficult because very few reference compounds are known. However, preliminary investigations were made by reducing the dinitro-compounds derived from base (III) without affecting the azo-group and converting

[12] Wohlfahrt, *J. prakt. Chem.*, 1902, **65**, 295.
[13] Ullmann and Dieterle, *Ber.*, 1904, **37**, 23.
[14] Täuber, *Ber.*, 1891, **24**, 197.
[15] Duval, *Bull. Soc. chim. France*, 1910, **7**, 485.
[16] King and King, *J.*, 1945, 824.
[17] Ross and Kuntz, *J. Amer. Chem. Soc.*, 1952, **74**, 1297.
[18] Arcos and Miller, *J. Org. Chem.*, 1956, **21**, 652.
[19] Badger, Seidler, and Thomson, *J.*, 1951, 3207.
[20] Täuber, *Ber.*, 1895, **28**, 451.

XUM

the resulting diamines into dibromo-derivatives. Neither was identical with 5,10-dibromobenzo[*f*]naphtho[2,1-*c*]cinnoline which was synthesised unambiguously by the reduction of 4,4′-dibromo-2,2′-dinitro-1,1′-binaphthyl. As the protonated azo-group is *meta*-directing, it is unlikely that the nitro-groups are in the 6,9-positions; presumably they are in the outer rings, the protonated azo-group having deactivated the rings adjacent to the pyridazine ring. The complete determination of the orientation must await the synthesis of relevant derivatives in the binaphthyl series.

These and other polycyclic cinnolines give intense colours with concentrated sulphuric acid. Progressive dilution of the coloured solution with water first changes the colour, then precipitates the original cinnoline. For example, compound (III) gives a purple solution in concentrated sulphuric acid but a yellow solution in aqueous sulphuric acid.

Experimental

Halogenonitroarenes.—These compounds were prepared by the Sandmeyer procedure according to published methods, except for the following details: 6-halogeno-1,2,3,4-tetrahydro-7-nitronaphthalenes are prepared in better yield if the amines are diazotised in hydrochloric rather than sulphuric acid.

6-Chloro-1,2,3,4-tetrahydro-7-nitronaphthalene (0·18 g.) is precipitated when the diazonium salt from 6-amino-1,2,3,4-tetrahydro-7-nitronaphthalene (0·2 g.) in 1 : 1 hydrochloric acid (30 ml.) is added to cuprous chloride (1 g.) in concentrated hydrochloric acid (20 ml.). Purified by chromatography from acetone on alumina, it gives pale yellow needles (from acetone), m. p. 54·5° (Found: C, 57·2; H, 4·5; N, 6·1. $C_{10}H_{10}O_2NCl$ requires C, 56·8; H, 4·7; N, 6·6%).

1-Iodo-2-nitronaphthalene. 1-Acetamidonaphthalene (80 g.) was nitrated and partially hydrolysed [21] to 1-amino-4-nitronaphthalene, which is partially precipitated, and 1-acetamido-2-nitronaphthalene. The published method of separating the latter is unsatisfactory. It was easily separated and hydrolysed as follows. Water was added to the filtered solution. The precipitate was separated, dried at 70°, and dissolved in hot acetone. The filtered solution yielded 1-acetamido-2-nitronaphthalene (20 g.), m. p. 198—200° (lit., m. p. 199°), on cooling. To 1-acetamido-2-nitronaphthalene (39 g.) in boiling ethanol (1300 ml.) was added hydrochloric acid (800 ml.). After 12 hours' refluxing, hydrochloric acid (200 ml.) and ethanol (200 ml.) were added and refluxing was continued for 6 hr. The solution precipitated 1-amino-2-nitronaphthalene (30 g.) on cooling, which was converted into 1-iodo-2-nitronaphthalene.[22]

Dinitrobiaryls.—Activated copper bronze was added to an equal weight of the halogenonitro-compound in boiling dimethylformamide. After 4 hr. more copper bronze was added and refluxing continued. After a further 2 hr. the mixture was filtered, the residue was extracted with ethanol, benzene, or dimethylformamide, and the extract boiled with charcoal and filtered. The filtrate was concentrated to give a crystalline product. By this means the following biaryls were prepared: 2,2′-dinitro-1,1′-binaphthyl (8·9 g.), m. p. 177°, from 1-iodo-2-nitronaphthalene (20 g.); 1,1′-dinitro-2,2′-binaphthyl (9 g.), m. p. 285° (lit.,[8] m. p. 284°), from 2-iodo-1-nitronaphthalene (20 g.), and 5,6,7,8,5′,6′,7′,8′-octahydro-3,3′-dinitro-2,2′-binaphthyl (20 mg.), m. p. 195° (lit., m. p. 201°), from 1,2,3,4-tetrahydro-6-iodo-7-nitronaphthalene (150 mg.).

1-Chloro-2,6-dinitrobenzene (3 g.), gave *m*-dinitrobenzene (1·5 g.), m. p. 87°; and 9-bromo-10-nitrophenanthrene (2 g.) gave 9-nitrophenanthrene (1·2 g.), m. p. 115° (lit., m. p. 116°) [picrate, m. p. 98—99° (lit., m. p. 98—99°)]. In the absence of copper powder, 9-bromo-10-nitrophenanthrene was recovered unchanged.

In two other cases better yields were obtained without dimethylformamide, as follows. Activated copper bronze (3 g.) was added in small portions to the heated (150—160°) 4-bromo-1-iodo-2-nitronaphthalene [23] (2 g.) during 40 min. The cooled mass was repeatedly extracted with ethanol and the extracts were boiled with charcoal, filtered, and concentrated to give *4,4′-dibromo-2,2′-dinitro-1,1′-binaphthyl* (0·1 g.), yellow rhombs (from acetone), m. p. 241° (Found: C, 47·8; H, 2·0; N, 5·65; Br, 31·9. $C_{20}H_{10}ON_2Br_2$ requires C, 47·8; H, 2·0; N, 5·58; Br, 31·9%).

[21] Hodgson and Walker, *J.*, 1933, 1205.
[22] *Idem*, *J.*, 1933, 1620.
[23] Meldola and Desch, *J.*, 1892, **61**, 765.

9-Bromo-10-nitrophenanthrene [24] (2 g.) was similarly treated, but in this case the temperature was slowly raised to 200°. From an extract in toluene was obtained 10,10′-*dinitro*-9,9′-*biphenanthryl* (80 mg.), pale brown crystals (from toluene solution filtered through alumina), m. p. 345° (decomp.) (Found: C, 75·8; H, 4·1; N, 6·1. $C_{28}H_{16}O_4N_2$ requires C, 75·8; H, 3·6; N, 6·3%).

Reduction of Dinitrobiaryls with Lithium Aluminium Hydride.—*2,2′-Dinitro-1,1′-binaphthyl.* Lithium aluminium hydride (2 g.) in ether (200 ml.) was added dropwise to 2,2′-dinitro-1,1′-binaphthyl (3 g.) in ether (500 ml.). After 45 min. water was added. The resulting precipitate was filtered off and extracted with ether. The extract and filtrate were concentrated to 200 ml., then extracted with 1 : 1 hydrochloric acid. The extract was made alkaline, and the resulting precipitate was washed with ether and recrystallised from acetone, to give compound (III) (0·6 g.), m. p. 270° (lit., m. p. 267—268°). A red tar is also produced which appears to be a complex mixture of azo-compounds. The base (III) is soluble in organic liquids and in acids. From acid solution it is reprecipitated by alkali. It forms a colourless solution when boiled with zinc dust and hydrochloric acid but the product is readily oxidised to the original substance. With saturated picric acid in ethanol, compound (III) gave *benzo*[f]*naphtho*[2,1-c]*cinnoline monopicrate*, m. p. 182° (Found: C, 60·7; H, 3·15; N, 13·0. $C_{26}H_{15}O_7N_5$ requires C, 61·4; H, 2·95; N, 13·8%).

4,4′-Dibromo-2,2′-dinitro-1,1′-dinaphthyl (70 mg.) was reduced by a similar procedure; the product, purified chromatographically on alumina, gave 5,10-*dibromobenzo*[f]*naphtho*[2,1-c]*cinnoline* (11 mg.), yellow needles (from acetone), m. p. 277° (Found: C, 54·2; H, 1·9. $C_{20}H_{10}NBr_2$ requires C, 54·8; H, 2·3%).

The substance (III) (125 mg.) in ethanol (150 ml.) when refluxed with methyl iodide (40 ml.) for 7 hr. yielded *benzo*[f]*naphtho*[2,1-c]*cinnoline methotri-iodide* (210 mg.) as red blades with a copper lustre (from acetone), m. p. 207° (Found: C, 37·0; H, 2·4; N, 4·05; I, 56·8. $C_{21}H_{15}N_2I_3$ requires C, 37·3; H, 2·2; N, 4·1; I, 56·3%).

Reduction of compound (III) (44 mg.) with sodium amalgam in methanol gave 2,2′-diamino-1,1′-binaphthyl (31 mg.), m. p. 184°, mixed with 2,2′-diamino-1,1′-binaphthyl (m. p. 191°) m. p. 191°.

1,1′-Dinitro-2,2′-binaphthyl.—Dinitrobinaphthyl (3 g.) and benzene (500 ml.) were dried by distillation until about 150 ml. of benzene were removed. Lithium aluminium hydride (3 g.) in ether (200 ml.) was added and the mixture was refluxed for 15 min., then stirred at room temperature during 4 hr. Water was added and the solution filtered. The filtrate was concentrated to give crystals, which were recrystallised from acetic acid, of *benzo*[h]*naphtho*[1,2-c]*cinnoline* (I), yellow needles (from acetone), m. p. 266°. A red-green dichroic solution was given in concentrated sulphuric acid (Found: C, 85·3; H, 4·0; N, 9·1. $C_{20}H_{12}N_2$ requires C, 85·7; H, 4·3; N, 10·0%). It gave a *hemipicrate*, m. p. 245° (decomp.) (Found: C, 69·8; H, 3·5; N, 12·8. $C_{46}H_{27}O_7N_7$ requires C, 70·0; H, 3·4; N, 12·4%).

Reduction of compound (I) (24 mg.) with sodium amalgam in methanol gave 1,1′-diamino-2,2′-binaphthyl (14 m.g), m. p. 273°, mixed m. p. 273°. Reduced with zinc dust in acetic acid, the base (I) (33 mg.) gave dibenz[*a*,*i*]carbazole (16 mg.), m. p. 211° [lit., m. p. 216°; picrate, m. p. 237° (lit., m. p. 238°)]. Reduced with lithium aluminium hydride, the base (I) (36 mg.) gave a dihydrobenzo[*h*]naphtho[1,2-*c*]cinnoline (14 mg.), m. p. 186°.

When the reduction of 1,1′-dinitro-2,2′-binaphthyl was continued under reflux for 18 hr. the addition of water and filtration gave a pale green fluorescent filtrate which, with hydrochloric acid (1 ml.) yielded a red precipitate. The separated solid was washed with benzene and boiled with aqueous ammonia. It gave 5(?),6(?)-*dihydrobenzo*[h]*naphtho*[1,2-c]*cinnoline* (0·5 g.) as yellow rhombs (from acetone), m. p. 186—187° (Found: C, 84·6; H, 4·8; N, 9·0. $C_{20}H_{14}N_2$ requires C, 85·1; H, 5·0; N, 9·9%). The compound, *e.g.*, in acetone, was oxidised in air to the parent cinnoline.

5,6,7,8,5′,6′,7′,8′-Octahydro-3,3′-dinitro-2,2′-binaphthyl.—The binaphthyl (21 mg.), reduced by a similar method, gave a product which after chromatography on alumina yielded yellow needles (from benzene) of 2,3,4,5,9,10,11,12-*octahydrobenzo*[g]*naphtho*[2,3-c]*cinnoline* (8 mg.), m. p. 264° (Found: C, 82·8; C, 6·75. $C_{20}H_{20}N_2$ requires C, 83·3; H, 6·95%).

10,10′-Dinitro-9,9′-biphenanthryl (30 mg.), reduced similarly, gave a yellow substance which did not melt at 360° and was different from the compound reported [2] as being (IV), m. p. 290°. Insufficient material was obtained for analysis.

[24] Callow and Gulland, *J.*, 1929, 2424.

Reduction with Sodium Amalgam and Methanol.—*2,2′-Dinitro-1,1′-binaphthyl.* Sodium amalgam (2%; 100 g.) was added to the binaphthyl (1 g.) in methanol (300 ml.). After 12 hr. the mixture was concentrated. The precipitate formed when the solution cooled was identified as 2,2′-diamino-1,1′-binaphthyl (0·7 g.), colourless crystals (from benzene–light petroleum), m. p. 190° (lit., m. p. 187°) [acetyl derivative, m. p. 228° (lit., m. p. 235—236°)]. 1,1′-Dinitro-2,2′-binaphthyl in benzene (400 ml.), reduced similarly, gave 1,1′-diamino-2,2′-binaphthyl (0·5 g.), m. p. 273° (lit., m. p. 281°) [acetyl derivative, m. p. 227° (lit., m. p. 229—230°)].

Reduction with Sodium Sulphide.—2,2′-Dinitro-1,1′-binaphthyl (1·4 g.) in ethanol (200 ml.) with hydrated sodium sulphide (2 g.), sodium hydroxide (0·5 g.), and water (20 ml.) was refluxed for 3 hr., concentrated to 100 ml., and poured into water. The resulting precipitate recrystallised from acetone as yellow needles (0·85 g.), identified as benzo[*f*]naphtho[2,1-*c*]cinnoline *N*-oxide, m. p. 252° [lit., m. p. 247—248° (decomp.)] (Found: O, 5·4. $C_{20}H_{12}ON_2$ requires O, 5·4%). Reduction of the oxide with stannous chloride or with lithium aluminium hydride gave base (III).

1,1′-Dinitro-2,2′-dinaphthyl (1 g.) was dissolved in benzene (400 ml.), then reduced with sodium sulphide as above after addition of ethanol (400 ml.). The product gave yellow needles (from acetone) of benzo[*h*]naphtho[1,2-*c*]cinnoline *N*-oxide (0·22 g.), m. p. 255—257°, mixed with specimen formed from the cinnoline (see below) m. p. 258°. Reduction of the oxide with stannous chloride or lithium aluminium hydride gave base (I).

Reduction with Zinc Dust and Potassium Hydroxide.—To 2,2′-dinitro-1,1′-binaphthyl (2 g.) in ethanol (600 ml.) was added potassium hydroxide solution, then zinc dust (25 g.). After refluxing for 30 min. the solution, when concentrated, yielded benzo[*f*]naphtho[2,1-*c*]cinnoline (1·2 g.), m. p. 258—260° (lit., m. p. 267—268°), which gave a purple colour with sulphuric acid (*d* 1·84). With less zinc (10 g.), benzo[*f*]naphtho[2,1-*c*]cinnoline *N*-oxide (0·6 g.), m. p. 246° (lit., m. p. 247—248°), was obtained, which gave a brown colour with sulphuric acid.

By a similar method (large excess of zinc) 4,4′-dibromo-2,2′-dinitro-1,1′-binaphthyl gave benzo[*f*]naphtho[2,1-*c*]cinnoline (7·5 mg.), m. p. and mixed m. p. 261° (lit., m. p. 267°) {mixed with 5,10-dibromobenzo[*f*]naphtho[2,1-*c*]cinnoline, m. p. 220—230°}.

1,1′-Dinitro-2,2′-dinaphthyl (1 g.) required refluxing for 4 hr. to give benzo[*h*]naphtho[1,2-*c*]-cinnoline (0·34 g.), m. p. 263—265°, which gave a red-green dichroic solution in sulphuric acid. 10,10′-Dinitro-9,9′-diphenanthryl required a reduction time of 14 hr. The precipitate was separated and extracted with ethanol (which removed unchanged diphenanthryl), then with chloroform. The chloroform solution gave yellow needles which did not melt at 360°, in too small a yield for analysis. The product gave a deep blue colour with sulphuric acid.

Oxidation of Cinnolines with Hydrogen Peroxide.—Hydrogen peroxide (80%; 2 ml.) was added to compound (III) (67 mg.) in acetic acid (20 ml.) at 0°. After 18 hr. and on concentration, benzo[*f*]naphtho[2,1-*c*]cinnoline *N*-oxide (47 mg.), m. p. and mixed m. p. 252·5°, was precipitated. By a similar process benzo[*c*]cinnoline (75 mg.) gave its *N*-oxide (35 mg.), m. p. 140° (lit., m. p. 139°). Compound (I) (0·16 g.) gave *benzo*[h]*naphtho*[1,2-c]*cinnoline N-oxide* (0·11 g.), yellow needles (from ethanol or acetone), m. p. 259° (Found: C, 80·8; H, 4·4; N, 9·6. $C_{20}H_{12}ON_2$ requires C, 81·0; H, 4·1; N, 9·45%).

Nitration of Compound (III).—The compound (III) (1 g.) was nitrated at 18° with nitric acid (*d* 1·5; 5 ml.) for 2 days. w,x-*Dinitrobenzo*[f]*naphtho*[2,1-c]*cinnoline* (0·24 g.) separated, giving yellow rhombs (from nitrobenzene), m. p. 337° (Found: C, 64·2; H, 2·9; N, 14·5. $C_{20}H_{10}O_4N_4$ requires C, 64·8; H, 2·7; N, 15·1%). With stannous chloride (1 g.) in hydrochloric acid (50 ml.) at 100°, the dinitro-compound (0·24 g.) gave impure *w,x*-diaminobenzo[*f*]naphtho[2,1-*c*]-cinnoline hemihydrate (62 mg.) as dark red needles (from aqueous dimethylformamide), m. p. 360° [Found: C, 74·2; H, 4·7. Calc. for $C_{20}H_{10}N_2(NH_2)_2,\frac{1}{2}H_2O$: C, 75·2; H, 4·7. Calc. for $C_{20}H_{10}N_2(NH_2)_2$: C, 77·5; H, 4·5. Calc. for $C_{20}H_{10}N_2(NH_2)\cdot NO_2$: C, 70·7; H, 3·55%). The tetrazotised diamine (60 mg.), when treated with cuprous bromide in hydrobromic acid, gave w,x-*dibromobenzo*[f]*naphtho*[2,1-c]*cinnoline* (11 mg.) as yellow plates (from acetone–ethanol), m. p. 293—297° {mixed m. p. with 5,10-dibromobenzo[*f*]naphtho[2,1-*c*]cinnoline (m. p. 277°) 230—245°} (Found: C, 52·7; H, 2·3; N, 6·2; Br, 35·5. $C_{20}H_{10}N_2Br_2$ requires C, 54·8; H, 2·3; N, 6·4; Br, 36·6%).

The filtrate from the nitration of compound (III) was left at 18° for 2 days. y,z-*Dinitrobenzo*[f]*naphtho*[2,1-c]*cinnoline* (0·22 g.) separated as pale yellow needles (from nitrobenzene), m. p. 324° {mixed with *w,x*-dinitrobenzo[*f*]naphtho[2,1-*c*]cinnoline, m. p. 280—290°} (Found: C, 65·7; H, 2·6; N, 14·8. $C_{20}H_{10}O_4N_2$ requires C, 64·8; H, 2·7; N, 15·1%). With stannous

chloride (0·5 g.) in hydrochloric acid the dinitro-compound (30 mg.) was reduced and the solution gave a red powder with excess of alkali; this product was passed in solution in ethanol through an alumina column. The diluted eluate gave y,z-*diaminobenzo*[f]*naphtho*[2,1-c]*cinnoline hemihydrate*, m. p. 296° [Found: C, 75·6; H, 5·1. $C_{20}H_{10}N_2(NH_2)_2,\frac{1}{2}H_2O$ requires C, 75·2; H, 4·7%].

Nitration of Compound (I).—To the base (0·1 g.) was added nitric acid (*d* 1·5; 1·5 ml.) at 0°. The mixture was kept 6 days at 18°. The resulting x,y-*dinitrobenzo*[h]*naphtho*[1,2-c]*cinnoline* (90 mg.) was filtered off, and formed yellow crystals (from nitrobenzene), m. p. 345° (Found: C, 64·3; H, 2·84; N, 14·3%).

The authors are grateful to Mr. F. Oliver for an oxygen analysis, and one of them (R. S. W. B.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

THE UNIVERSITY, READING. [*Received, March 6th*, 1959.]

---

606. *Aromatic Reactivity. Part V.* Desilylations of Trimethylsilyldiphenyls.*

By F. B. DEANS, C. EABORN, and D. E. WEBSTER.

The influence of a phenyl substituent on the reactivity of a benzene ring towards electrophilic substitution has been studied for desilylations of *o*-, *m*-, and *p*-trimethylsilyldiphenyl. The results show that an *o*- or *p*-Ph substituent has an activating and a *m*-Ph substituent a deactivating effect, and considered along with data for electrophilic substitutions in diphenyl itself they indicate that the polar effect of either the *m*- or the *p*-phenyl group is too variable to be represented satisfactorily by a single substituent constant.

DESILYLATION of substituted phenyltrimethylsilanes provides a measure of the effects of nuclear substituents on the reactivity of a benzene ring towards electrophilic reagents.[1] This paper is concerned with the influence of *o*-, *m*-, and *p*-Ph substituents as revealed in the ease of cleavage of *o*-, *m*-, and *p*-trimethylsilyldiphenyl by (i) sulphuric acid–acetic acid–water at 50·18° (in which the attacking electrophile is an oxonium ion or related positive species),[1c] (ii) bromine in 1·5 wt.-% water–acetic acid at 25° (in which the electrophile is the bromine molecule or related neutral species),[1d] and (iii) mercuric acetate in 20 wt.-% water–acetic acid at 25° in which the electrophile is probably the $AcO{\cdot}Hg^+$ ion or similar species (cf. ref. 1*h*).

The results are expressed in the Table as rate factors, *f*, for the rate of desilylation relative to that of the parent compound, phenyltrimethylsilane. The corresponding partial rate factors for some substitutions in diphenyl are given for comparison, namely: (i) nitration by nitric acid in acetic anhydride; [2] (ii) deuteration in the system $CH_3{\cdot}CO_2D$–D_2SO_4–CCl_4; [3] (iii) acid-catalysed bromination by hypobromous acid in aqueous dioxan (involving a positive bromine species, Br^+ or $BrOH_2^+$); [2a] (iv) chlorination in acetic acid (involving molecular chlorine).[4] Corresponding figures for methyl substituents are listed for comparison.

It will be seen that in all cases the phenyl group activates *ortho*- and *para*-positions and, for all the cases in which the figures are available, deactivates the *meta*-position.

* Part IV, *J.*, 1959, 2303.

[1] (*a*) Eaborn, *J.*, 1953, 3148; (*b*) Eaborn, *J.*, 1956, 4588; (*c*) Deans and Eaborn, *J.*, 1959, 2299; (*d*) Eaborn and Webster, *J.*, 1957, 4449; (*e*) Benkeser and Krysiak, *J. Amer. Chem. Soc.*, 1954, **76**, 6353; (*f*) Benkeser, Hickner, and Hoke, *ibid.*, 1958, **80**, 2279; (*g*) Benkeser, Hickner, Hoke, and Thomas, *ibid.*, p. 528; (*h*) Benkeser, Hoke, and Hickner, *ibid.*, p. 5294.

[2] (*a*) de la Mare and Hassan, *J.*, 1957, 3004; (*b*) Dewar, Mole, and Warford, *J.*, 1956, 3576, 3581.

[3] Dallinga, Verrijn Stuart, Smit, and Mackor, *Z. Elektrochem.*, 1957, **61**, 1019.

[4] de la Mare, Hall, Harris, and Hassan, *Chem. and Ind.*, 1958, 1086.

XUM

These facts are in accord with representation [2a] of the phenyl group as withdrawing electrons by an inductive effect but returning electrons directly to *ortho*- and *para*-positions by an electromeric effect at the demand of the reagent (and possibly, though much less effectively, to the *meta*-position by secondary relay). Calculations of the free-valence number [5] and atom localisation energy [6] (which are more applicable to free-radical substitutions) indicate that *ortho*- and *para*-positions in diphenyl should be activated and the *meta*-position slightly deactivated. Using the Wheland model [7] for aromatic substitution Dewar calculates that *ortho*- and *para*-positions should be activated to about the same extent and the *meta*-position unaffected.[8] Calculation by the self-consistent field method of the energy required to convert the hydrocarbon ArH into the ion ArH_2^+ indicates that the *ortho*- and *para*-positions should be activated to about the same extent and that the *meta*-position should be slightly activated.[3]

The effect of a *p*-Ph group depends very much on the reaction concerned. This can be seen most effectively by considering the ratio $(\log f_p^{Me})/\log f_p^{Ph})$ (which is equivalent to considering the ratio of the effects of *p*-Me and *p*-Ph substituents on the free energies of activation). It will be seen (Table) that the ratio varies from 2·82 to 1·05, and it is clear that no single substituent constant of the Hammett type [10] can adequately represent the

Rate factors for phenyl and methyl substituents.

Reaction	*o*-Ph	*m*-Ph	*p*-Ph	*o*-Me	*m*-Me	*p*-Me	$\frac{\log f_p^{Me}}{\log f_p^{Ph}}$	Notes
Protodesiln.	6·0	0·33	2·8	15	2·2	18	2·82	(*a*)
Bromodesiln.	1·18	0·41	12·5	82	2·9	49	1·54	(*b*)
Mercuridesiln.	2·5	0·58	3·3	~11	2·5	17·5	2·40	—
Nitration	18·5	—	11·0	42	2·5	58	1·70	(*c*)
Bromination (Br^+)	10·7	0·28	15·6	76	2·5	59	1·48	(*d*)
Deuteration	37	(>0·3)	37	350	—	350	1·62	(*e*)
Chlorination	338	—	595	617	4·95	820	1·05	(*f*)

(*a*) The figure for *p*-Me is from ref. 1*c*, and those for *m*-Me and *p*-Me are deduced from data for $HClO_4$–MeOH–H_2O in ref. 1*b*. (*b*) Data for the tolyl compounds are from ref. 1*d*. (*c*) Figures for diphenyl are derived in ref. 2*a* from data in ref. 2*b*. Values of 41, <0·6, and 38 have also been given for *o*-, *m*-, and *p*-positions of diphenyl in nitration in acetic anhydride (Simamura and Mizuno, *Bull. Chem. Soc. Japan*, 1957, **30**, 196). (*d*) Data from ref. 2*a*. (*e*) Data for diphenyl are from ref. 3. Data for toluene are from Mackor, Smit, and van der Waals (*Trans. Faraday Soc.*, 1957, **53**, 1309), and actually refer to de-deuteration in $CF_3{\cdot}CO_2H$–H_2SO_4. (*f*) Data for diphenyl are from ref. 4 and for toluene from Brown and Stock (*J. Amer. Chem. Soc.*, 1957, **79**, 5175).

effect of the *p*-Ph substituent in electrophilic aromatic substitutions.* Similar variations are found if the corresponding ratios for *m*-Me and *m*-Ph or *m*-Ph and *p*-Ph substituents are taken, and it seems that the effect of the *m*-Ph group also cannot be represented by a single substituent constant.

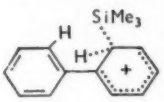
The ratio $(\log f_p^{Me})/(\log f_p^{Ph})$ is markedly smaller for bromodesilylation than for proto- and mercuri-desilylation, probably because electromeric release of electrons by the phenyl group is called forth more strongly by a neutral reagent (with its greater electron-demand) than by a positive one.[2a,10] It is of interest that in the Table the highest values of the ratio are associated with the lowest values of f_p^{Me}, *i.e.*, with the smallest electron-demand as roughly indicated by the activating effect of the *p*-Me group. The lowest value of the

* The ratio of the (σ^+) substituent constants proposed for the *p*-Me and *p*-Ph groups in electrophilic reactions,[9] which should agree with observed $(\log f_p^{Me}/\log f_p^{Ph})$ ratios, is 1·74.

[5] Burkitt, Coulson, and Longuet-Higgins, *Trans. Faraday Soc.*, 1951, **47**, 553.
[6] Seel, *Z. Elekrochem.*, 1948, **52**, 191.
[7] Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900.
[8] Dewar, *ibid.*, 1952, **74**, 3341 *et seq.*; Dewar, *J.*, 1952, 3544; Dewar, Mole, and Warford, *J.*, 1956, 3581.
[9] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979.
[10] de la Mare and Harvey, *J.*, 1956, 36; 1957, 131.

ratio, that for molecular chlorination, is correspondingly associated with the highest value of f_p^{Me}. Intermediate figures show an appropriate general trend, though with obvious deviations.

Satisfactory interpretation of the effects of *o*-Ph substituents is not yet possible. The simplest explanation of the large activation by an *o*-Ph group compared with that by *p*-Ph group in protodesilylation is that in *o*-trimethylsilyldiphenyl steric interaction between the Me_3Si group of one ring and the *o*-hydrogen atoms of the other ring prevents co-planarity of the rings, and thus hinders conjugation between the activating phenyl group and other ring to a greater extent than it is hindered in diphenyl itself. In a transition state approximating to the intermediate (I), the tetrahedral disposition of bonds around the carbon atom participating in the aryl–$SiMe_3$ bond may allow the two rings to become coplanar (as presumably they do during reaction of the *p*-Ph isomer). (Substitutions in diphenyl itself involve the same initial state whatever the position attacked, and different considerations apply.) The high reactivity of the *ortho*-isomer may thus be attributed mainly to destabilization of the initial state (by as little as 0·5 kcal. mole^{-1}). Trapping of the *o*-hydrogen atom of the activating phenyl group between the hydrogen atom and Me_3Si group at the attacked carbon may in addition somewhat stabilize the transition state by enforcing (as distinct from permitting) coplanarity of the rings.*



(I)

Such an explanation neglects the effects of entropy changes, which may be considerable. A structure such as (I), in which a hydrogen atom of the activating phenyl group is constrained between the entering and the leaving group, would be very rigid, and there would be an unfavourable entropy change on going from the initial state to a transition state similar to the intermediate. It is possible that the abnormally low reactivity of *o*-trimethylsilyldiphenyl in bromodesilylation arises from an entropy change more unfavourable than that in protodesilylation, the difference originating in the differing sizes and shapes of the entering group and in a differing balance of bond-making and bond-breaking processes.

Experimental

The preparations of the trimethylsilyldiphenyls have been described.[1c]

The procedure for measuring the substituent effects in bromodesilylation was identical with that previously employed.[1d]

An account of studies of mercuridesilylation reactions will be presented later. The conditions are such that reaction is of first order with respect to both the aromatic compound and the mercuric acetate. The results for this reaction are less accurate that those for the other desilylations.

We thank the Department of Scientific and Industrial Research for a maintenance grant (to D. E. W.), and Imperial Chemical Industries Limited for a grant towards the cost of chemicals.

The University, Leicester. [*Received, March 4th*, 1959.]

* Trapping of the activating phenyl group between the entering nitronium ion and the leaving hydrogen atom was postulated to explain the high reactivity of the *ortho*-position relative to that of the *para*-position in nitration of diphenyl in acetic acid (see Table).[2a] The difficulty of generalizing this explanation is seen when it is realized that towards nitration by mixed acid at 35—40° the *ortho*-position is less reactive than the *para*.[11]

[11] Jenkins, McCullough, and Booth, *Ind. Eng. Chem.*, 1930, **22**, 31; de la Mare and Hassan, *J.*, 1958, 1519.

XUM

607. *Aromatic Reactivity. Part VI.* Desilylations of α- and β-Trimethylsilylnaphthalene.*

By C. Eaborn, Z. Lasocki, and D. E. Webster.

We have measured the rates of proto- and bromo-desilylation of α- and β-trimethylsilylnaphthalene and of mercuridesilylation of the latter. The results are compared with those for nitration and deuteration of naphthalene. In these electrophilic aromatic substitutions the α- is more reactive than the β-position, but particularly so in the desilylations because of steric acceleration.

We have examined the reactivity of α- and β-trimethylsilylnaphthalene in protodesilylation [1,2] and bromodesilylation [3] and of the β-isomer in mercuridesilylation (reactions which are electrophilic aromatic substitutions [1-4]). The results are given in the Table as the rate of reaction, f, relative to that of phenyltrimethylsilane. Partial rate factors are also given for the α- and the β-positions of naphthalene in nitration in acetic anhydride,[5] and in deuteration in the medium $CF_3 \cdot CO_2H - H_2SO_4 - CCl_4$.[6] Effects of *o*- and *p*-methyl groups are included for comparison.

Reaction	α-$C_{10}H_7$	β-$C_{10}H_7$	*o*-Me	*p*-Me	$\frac{\log f_p^{Me}}{\log f_\beta}$	$\frac{\log f_\alpha}{\log f_\beta}$	Notes
Protodesiln.	8·1	2·16	18	21	3·96	2·72	(*a*)
Bromodesiln.	196	12·5	82	49	1·54	2·09	(*b*)
Mercuridesiln.	—	2·9	—	17·5	2·69	—	
Nitration	550	54	42	58	1·02	1·58	(*c*)
Deuteration	178	24	350	350	1·84	1·63	(*d*)

(*a*) Data for tolyl compounds are from ref. 1. (*b*) Figures for the tolyl compounds are from ref. 3 and from unpublished work by D. E. Webster. (*c*) Figures for naphthalene are calculated from data in ref. 5, and figures for toluene are from Cohn, Hughes, and Ingold (*Nature*, 1952, **169**, 291). (*d*) Data for naphthalene are from ref. 6; data for toluene actually refer to de-deuteration in $CF_3 \cdot CO_2H - H_2SO_4$ (Mackor, Smit, and van der Waals, *Trans. Faraday Soc.*, 1957, **53**, 1309).

In all cases the α- is more reactive than the β-position. The β-position is less reactive than the *para*-position of the corresponding diphenyls in all three desilylations and in deuteration. (The partial rate factors for the *para*-position of diphenyl are 3·5 in protodesilylation,[1] 12·5 in bromodesilylation,[2] 3·3 in mercuridesilylation,[7] and 37 in deuteration [6].) This is in accord with calculations by the self-consistent-field method of the energy required to convert the hydrocarbon ArH into its conjugate acid ArH_2^+ [6] (which represents a reasonable approximation to the transition state in electrophilic aromatic substitutions) and with calculations of atom localization energies.[5] In nitration the β-position of naphthalene appears to be more reactive than the *para*-position of diphenyl, for which a partial rate factor of 11 has been calculated [8] from Dewar, Mole, and Warford's data.[5] However, the nitration figures, based on difficult competitive studies, may be inaccurate, and another study of the nitration of diphenyl under similar conditions gave a factor of 38 for the *para*-position.[9]

For each reaction, activation of the β-position, f_β, is compared with activation by a *p*-Me group f_p^{Me}, by means of the ratio $(\log f_p^{Me})/(\log f_\beta)$ (which is equivalent to examining

* Part V, preceding paper.

[1] Eaborn, *J.*, 1956, 4858.
[2] Deans and Eaborn, *J.*, 1959, 2299.
[3] Eaborn and Webster, *J.*, 1957, 4449.
[4] Benkeser, Hoke, and Hickner, *J. Amer. Chem. Soc.*, 1958, **80**, 5294.
[5] Dewar, Mole, and Warford, *J.*, 1956, 3576, 3581.
[6] Dallinga, Verrijn Stuart, Smit, and Mackor, *Z. Elektrochem.*, 1957, **61**, 1019.
[7] Deans, Eaborn, and Webster, preceding paper.
[8] de la Mare and Hassan, *J.*, 1957, 3004.
[9] Simamura and Mizuno, *Bull. Chem. Soc. Japan*, 1957, **30**, 196.

substituent effects on the activation free energy of the reaction). The ratio varies considerably, and if, as seems to be the case,[10] the effect of a *p*-Me group can be reasonably represented by a single (electrophilic) substituent constant, σ^+,[11] then activation of the β-position of naphthalene cannot be so represented. Within the group of desilylations the ratio $(\log f_p^{Me})/(\log f_\beta)$ is lowest for bromodesilylation, probably because the neutral reagent, with its greater electron-demands, calls forth the electromeric effect of the activating ring more strongly than do the positive reagents in proto- and mercuri-desilylation.[8,12]

Activation of the α-position relative to the β-position, as measured by the ratio $(\log f_\alpha)/(\log f_\beta)$, is greater in desilylations than in the other reactions. This is because there is steric acceleration of desilylations at the α-position, interference between the α-Me_3Si group and the *peri*-hydrogen atom being relieved in a transition state in which the disposition of the bonds to the α-carbon atom approximates to tetrahedral. It is interesting to note that the abnormally low reactivity of 2-trimethylsilyldiphenyl in bromodesilylation [7] is not reflected in the reactivity of α-trimethylsilylnaphthalene in this reaction. For the diphenyl compound the effect was tentatively attributed to an unfavourable entropy effect on passing to the transition state,[7] and such effects do not arise with the naphthalene compound for which the rigidity of the molecule does not differ much in the ground state and the transition state.

Experimental

α-Trimethylsilylnaphthalene was prepared from trimethylchlorosilane, α-chloronaphthalene, and sodium in boiling toluene. Fractional distillation gave material of b. p. 162°/30 mm., n_D^{20} 1·5812.

The β-isomer, b. p. 164·5/37 mm., n_D^{20} 1·5736, was prepared analogously.

Protodesilylation was studied, as previously described,[1] in a mixture of 5 vol. of a methanolic solution of the organosilane (0·00052M for the naphthalene compounds and 0·014M for phenyltrimethylsilane) and 2 vol. of 9·16M-perchloric acid at 50·0°. Reactions were studied at wavelengths of 231 and 264 mμ for phenyltrimethylsilane, 297 and 299 mμ for the α-naphthyl compound, and 292 and 239 mμ for the β-isomer. Isosbestic points of 262·5 and 240·2 mμ (α-isomer) and 286 and 246 mμ (β-isomer) were used to check the stability of the system (see ref. 1). First-order rate constants of 0·0145, 0·0039, and 0·000180 $min.^{-1}$ were found for the α-isomer, β-isomer, and phenyltrimethylsilane, respectively.

The bromodesilylations were examined in acetic acid containing 1·5 wt.-% of water at 25·0° as previously described.[8]

Mercuridesilylations involved mercuric acetate in acetic acid containing 20 wt.-% of water at 25·0°. Details will be published later.

We thank the Department of Scientific and Industrial Research for a Maintenance Grant (to D. E. W.) and the Polish Ministry of Education for a Research Fellowship (to Z. L.).

The University, Leicester. [*Received, March 23rd,* 1959.]

[10] Brown and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 6992; Nelson, *J. Org. Chem.*, 1956, **21**, 145; Lauer, Matson, and Stedman, *J. Amer. Chem. Soc.*, 1958, **80**, 6433.
[11] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979.
[12] de la Mare and Harvey, *J.*, 1956, 36; 1957, 131.

608. *The Reactivities of Substituted Benzophenones in Oxime Formation.*

By J. D. Dickinson and C. Eaborn.

We have measured the rates of acid-catalysed formation of oximes from some monosubstituted benzophenones in aqueous methanol. The effects of substituents are not in accord with their Hammett σ-constants, but can be interpreted if account is taken of loss of conjugation between aryl and carbonyl groups on passing from the ground state to the transition state.

We have measured spectrophotometrically the rates of acid-catalysed formation of oximes by some monosubstituted benzophenones in presence of excess of hydroxylamine hydrochloride in 70% methanol containing sodium acetate and acetic acid. First-order rate constants, k, are shown in Table 1, along with the apparent activation energies, E, and log A values.

Table 1. *Reaction of benzophenones,* $X{\cdot}C_6H_4{\cdot}CO{\cdot}C_6H_5$, *with hydroxylamine in acidic 70% methanol at 50°.*[a]

X	10^3k (min.$^{-1}$)	E (kcal./mole)	$\log_{10} A$ [b]	X	10^3k (min.$^{-1}$)	E (kcal./mole)	$\log_{10} A$ [b]
H	9·2	13·15	6·85	*m*-HO	8·7	13·0	6·7
p-Ph	8·3	13·55	7·05	*p*-HO	3·35	14·05	7·05
m-Me	9·05	13·3	6·95	*p*-Br	8·5	12·75	6·55
p-Me	7·3	13·6	7·05	*m*-NO_2 ...	9·65	11·75	5·9
m-MeO ...	9·0	13·15	6·85	*p*-NO_2	11·8	11·55	5·9
p-MeO	4·05	14·0	7·05				

[a] For exact medium see Experimental section. [b] $\log k = \log A - (2{\cdot}303\,E/RT)$.

The reaction is hindered by strongly electron-releasing groups such as *p*-MeO and *p*-OH, and facilitated, less effectively, by strongly electron-withdrawing substituents such

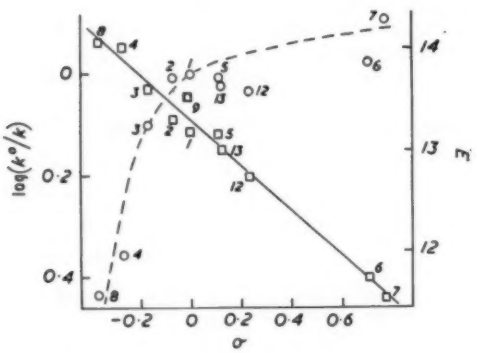


Fig. 1. *Plot of* log $(k°/k)$ *(circles) and of activation energy, E (squares) against* σ.
Substituents: 1, H; 2, *m*-Me; 3, *p*-Me; 4, *p*-MeO; 5, *m*-MeO; 6, *m*-NO_2; 7, *p*-NO_2; 8, *p*-HO; 9, *p*-Ph; 10, *p*-Cl; 11, *m*-Cl; 12, *p*-Br; 13, *m*-HO.

as *p*-NO_2, while *meta*-substituents have no significant effect. A plot of log $k°/k$ (where $k°$ is the rate of reaction of benzophenone) against the Hammett substituent constants, σ [1] (values of which are taken from ref. 2) shows a marked curvature (Fig. 1). A plot of σ against activation energy, E, is a straight line, but we cannot be certain that this is significant in view of the experimental uncertainty in E.

Curvature of log k–σ plots seems to be general for reactions involving addition to carbonyl groups in aryl carbonyl compounds. The curve goes through a maximum in

[1] Jaffé, *Chem. Rev.*, 1953, **53**, 191.
[2] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979.

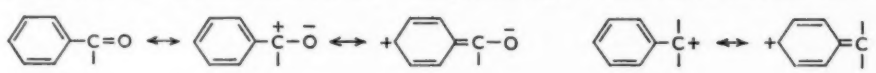
reaction of benzaldehydes with *n*-butylamine,[3] semicarbazide,[4] and hydrogen cyanide[5] (the logarithm of the equilibrium constant being plotted in the last case), but the existence of a maximum has no special significance since the curvatures are temperature-dependent, the entropies of activation not being constant for a series of substituents in a given reaction.[3] In formation of oximes from benzophenones, for example, if the values of E and log A in Table 1 are accurate, a maximum would be observed at 100°, while in reaction of benzaldehydes with butylamine there would be no maximum at 100° although one is observed at 25°.[3] The log k–σ plot is said to be a straight line in semicarbazone formation by *para*-substituted acetophenones,[6] but the correlation is rather unsatisfactory at the experimental temperature of 50° even for the small number of substituents examined, and on the basis of the reported log A and E values the plot, which has a negative slope at 50°, would have a positive slope at 25° and show a rate minimum at 0°. (A plot of E against σ approximates to a straight line, as with benzophenones.)

The curvature of the log k–σ plots in the benzaldehyde–*n*-butylamine and benzaldehyde–semicarbazide reactions, and particularly the occurrence of rate-maxima, have been attributed to the formation of intermediates.[3,4] It was not shown for the first reaction exactly why a maximum would result.[3] For the second, Noyce, Bottini, and Smith[4] postulated that the rate of return of the intermediate to the reactants was similar to the rate of its decomposition to products; in the general case $A \underset{(2)}{\overset{(1)}{\rightleftharpoons}} B \xrightarrow{(3)} C$, the rate of formation of C is given by $k = k_1k_3/(k_2 + k_3)$, where k_1, k_2, and k_3 are the specific rates of reactions (1), (2), and (3), respectively, and for a change from the unsubstituted compound to one having a substituent of substituent-constant σ, the rate change from k° to k is given by

$$\log (k/k^\circ) = (\rho_1 + \rho_3 - \rho_2)\sigma - \log\left[\left(1 + \frac{k_3^\circ}{k_2^\circ}10^{(\rho_3 - \rho_2)\sigma}\right)\Big/\left(1 + \frac{k_3^\circ}{k_2^\circ}\right)\right]$$

[where $\log (k_1/k_1^\circ) = \rho_1\sigma$, and so on]. This function is not linear in σ, and passes through a maximum. However, we believe that in practice the value of $(\rho_3 - \rho_2)$ will normally be too small for the log term to reverse the trend established by the $(\rho_1 + \rho_3 - \rho_2)$ term. Since, for this treatment, B must be an intermediate of high energy, and k_1 must be approximately equal to k_2, the transition states for reactions A ⟶ B and B ⟶ C are not far removed from the intermediate B, and are placed fairly symmetrically with respect to B, so that the effect of a change of structure will be rather similar on these transition states and on B.[7] The values of ρ_2 and ρ_3 will thus be small and rather similar, so the difference $(\rho_3 - \rho_2)$ will be very small and a linear log k–σ plot will result.

Another objection to the explanation advanced by Noyce *et al.* is that the return of the intermediate to reactants is unlikely to be comparable with the rate of its decomposition to products when ketones are involved,[3,4] and yet the log k–σ plots can be seriously curved



(I) (II) (III) (IV) (V)

as we have now shown. An explanation is required which is generally applicable to all of these carbonyl reactions, and we suggest that the common feature is that the conjugation between the aryl and the carbonyl groups [canonical forms (I), (II), and (III) are shown] has largely disappeared in the transition state of the rate-determining step. In oxime

[3] Santerre, Hansrote, and Crowell, *J. Amer. Chem. Soc.*, 1958, **80**, 1254.
[4] Noyce, Bottini, and Smith, *J. Org. Chem.*, 1958, **23**, 752.
[5] Branch and Calvin, "The Theory of Organic Chemistry," Prentice-Hall Inc., New York, 1941, pp. 347—351.
[6] Cross and Fugassi, *J. Amer. Chem. Soc.*, 1949, **71**, 223.
[7] Hammond, *ibid.*, 1955, **77**, 334.

XUM

formation this transition state probably lies between the benzophenone and the intermediate $Ph_2C(OH)\cdot NH\cdot OH$, subsequent dehydration being fast, but in general it is only necessary that the transition state is not greatly removed on the reaction co-ordinate from the intermediate of type $RR'C(OH)\cdot NHX$. The ordinary σ-constants do not serve to indicate the effects of substituents on the conjugation represented by resonance involving structures (II) and (III), but we suggest that the σ^+-constants, applicable to electrophilic reactions,[2] will so serve as an approximation, since by their derivation they reveal the effects of substituents on the analogous resonance involving (for example) structures (IV) and (V).* If the effect of the substituent were exerted only through this loss of conjugation then the relation $\log(k/k^\circ) = \rho_1\sigma^+$ would hold, the reaction being hindered by electron-releasing substituents. On the other hand, if there were no serious change in this conjugation on going from ground state to transition state the usual relation $\log(k/k^\circ) = \rho\sigma$ would hold. Overall the relation $\log(k/k^\circ) = \rho'\sigma^+ + \rho\sigma$ holds, or $\log(k^\circ/k) = \rho(x\sigma^+ - \sigma)$,

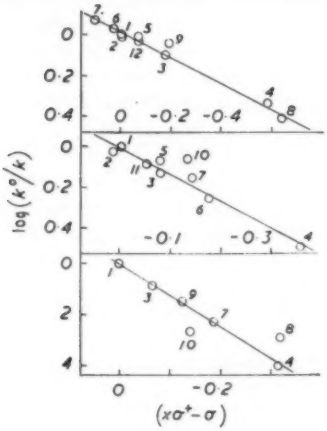


FIG. 2. *Plots of* $\log(k^\circ/k)$ *against* $(x\sigma^+ - \sigma)$ *for: (top) oxime formation by benzophenones* ($x = 1{\cdot}1$); *(centre) semicarbazone formation by benzaldehydes* ($x = 0{\cdot}8$); *(bottom) decomposition of benzenediazonium salts* ($x = 0{\cdot}75$).

1—13, As for Fig. 1.

where x is a constant and $\rho' = -x\rho$. Thus $\log(k^\circ/k)$ is proportional to $(x\sigma^+ - \sigma)$, and from values of $(x\sigma^+ - \sigma)$ listed in Table 2 it will be seen that plots of $\log(k^\circ/k)$ against σ may be seriously curved, or may go through a maximum, depending on the value of x.†

TABLE 2.[a]

Substituent	*p*-HO	*p*-MeO	*p*-Me	*m*-Me	*p*-Ph	*m*-MeO	*p*-Br	*m*-Cl	*m*-NO_2	*p*-NO_2
σ	−0·37	−0·268	−0·170	−0·069	−0·01	+0·115	+0·232	+0·373	+0·710	+0·778
σ^+	−0·92	+0·778	−0·311	−0·066	−0·179	+0·047	+0·150	+0·399	+0·674	+0·790
$(1{\cdot}1\sigma^+ - \sigma)$	−0·64	−0·580	−0·172	−0·004	−0·19	−0·063	−0·067	+0·066	+0·031	+0·091
$(0{\cdot}9\sigma^+ - \sigma)$	−0·46	−0·432	−0·110	+0·010	−0·17	−0·073	−0·097	−0·014	−0·103	−0·067
$(0{\cdot}7\sigma^+ - \sigma)$	−0·27	−0·277	−0·048	+0·023	−0·115	−0·082	−0·127	−0·093	−0·269	−0·225

[a] Values of σ^+ and σ are from ref. 2.

As required by our treatment, when $\log(k^\circ/k)$ is plotted against $(x\sigma^+ - \sigma)$ the points lie acceptably about a straight line for the benzophenone–hydroxylamine reaction ($x = 1{\cdot}1$) (Fig. 2). Comparable results are obtained for the benzaldehyde–semicarbazide reaction (Fig. 2) and the benzaldehyde–*n*-butylamine reaction ($x = 0{\cdot}6$).‡ In these three cases,

* It would probably be more correct to assume that the effect of a substituent on conjugation with the carbonyl group is indicated by $(\sigma^+ - \sigma)$, but in the present case the final conclusion would be the same.

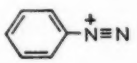
† We list figures only for a few relevant positive values of x. A positive x means that ρ and ρ′ have opposite signs, and thus that the carbonyl-additions immediately under consideration would be facilitated by electron-releasing substituents in absence of the special effects of conjugation.

‡ Deviations for *p*-halogeno- and *p*-phenyl substituents are not surprising since the σ^+-constants do not adequately represent the effects of these groups even in electrophilic reactions.[3]

[3] Eaborn, *J.*, 1956, 4858; Deans, Eaborn, and Webster, *J.*, 1959, 3031.

points for *meta*-substituents lie reasonably close to the line. This is not always to be expected, since *para*-substituents influence conjugation with side-chains directly, while *meta*-substituents operate only through a secondary relay of effects, and the stabilisation energy of the ground state may be related to σ^+ by a different proportionality constant in the two cases. For dissociation of benzaldehyde cyanohydrins [5] a plot of log K against $(0{\cdot}775\sigma^+ - \sigma)$ is satisfactory for *para*-substituents, but a separate plot is required for *meta*-substituents.

The treatment suggested above is applicable to some analogous cases. Thus the Curtius rearrangement of substituted benzoyl azides in toluene shows a rate maximum (both *p*-MeO and *p*-NO_2 groups, for example, deactivate) which has been qualitatively attributed to stabilisation of the ground state by electron-supplying substituents,[9] and we find that the points for *para*-substituents lie satisfactorily about a log (k°/k)–$(0{\cdot}75\sigma^+ - \sigma)$ plot. Perhaps the best known example of unusual effects of *para*-substituents is the decomposition of substituted benzenediazonium salts in aqueous acid,[10] and again these effects have been qualitatively attributed to ground-state stabilisation by groups having $+T$ effects.[11] In this case ground state stabilisation might be expected to follow σ^+ rather closely, since a positive charge in the conjugated side-chain is to be distributed [see structure (VI)]. On the other hand, in the ion (VII), which is formed in the rate-determining step, there cannot

(VI)  (VII)

be direct resonance between the π-electron system and the positively charged carbon since the π-orbitals are antisymmetric and the sp^2 carbon orbital is symmetric with respect to the plane of the ring, so that stabilisation of the ion (VII) (or of a transition state close to it) would be expected to follow σ and not σ^+. Thus a straight-line log (k°/k)–$(x\sigma^+ - \sigma)$ plot results (Fig. 2).

The type of treatment above is also applicable to some side-chain reactions of benzyl compounds which do not show satisfactory log k–σ correlation [12] [the reaction of benzyl chlorides with trimethylamine,[12] for example, for which a log (k°/k)–$(\sigma^+ - \sigma)$ plot is satisfactory for *para*-substituents]. In such reactions it is the transition state and not the ground state which has the extra resonance stabilisation.[13] We do not, however, propose to extend or refine out treatment,* because we believe it to be a simplified equivalent of a more fundamental division of substituent constants into inductive and resonance components now being developed by Taft and his co-workers.[14]

Experimental

The same stock solution of hydroxylamine hydrochloride in water (4·20M, as determined by titration [15]) was used throughout. Immediately before a run, 30 ml. of this solution were diluted to 100 ml. with methanol, and 10 ml. of this mixture were added to 10 ml. of a solution of the benzophenone (of concentration shown in Table 3) in " 70% methanol " (30 volumes of water diluted to 100 volumes with methanol) containing sodium acetate (0·20M) and acetic acid (0·20M). Some of the mixture thus obtained was transferred to a 1 cm. stoppered cell held in an Adkins thermostat in a Unicam S.P. 500 Spectrophotometer. After 15 min., to allow the

* We understand that Professor Yukawa is testing a similar treatment more extensively.

[9] Yukawa and Tsuno, *J. Amer. Chem. Soc.*, 1957, **79**, 5530.
[10] Crossley, Kienle, and Benbrook, *ibid.*, 1940, **62**, 1400.
[11] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons, Ltd., London, 1953, pp. 800—802: Bunnett and Zahler, *Chem. Rev.*, 1951, **49**, 273.
[12] Swain and Langsdorf, *J. Amer. Chem. Soc.*, 1951, **73**, 2813.
[13] Bartlett, in Gilman's " Organic Chemistry," Wiley and Sons, New York, Vol. III, 1953, pp. 33—35.
[14] Taft, " Steric Effects in Organic Chemistry " (Ed., M. S. Newman), Wiley and Sons, New York, 1956, Chapter 13; cf. Taft and Lewis, *J. Amer. Chem. Soc.*, 1958, **80**, 2436 and refs. therein.
[15] Vogel, " Quantitative Inorganic Analysis," Longmans, Green and Co., London, 2nd Edn., 1951, p. 375.

XUM

solution to reach the thermostat temperature (50·0° or 40·0°, maintained within ±0·03°), readings of the optical density were taken at the wavelengths, λ, shown in Table 3, and continued for 10 times the half-life period. The pH of the reaction mixture (5·02, measured directly with a glass electrode) was unchanged at the end of the reaction. Constancy of the first-order rate constants was excellent during more than 90% of reaction, and overall rate constants were reproducible within ±1%. Activation energies are believed to be accurate to within 0·4 kcal. mole^{-1}.

TABLE 3.

X (in X·C_6H_4·CO·C_6H_5)	H	*m*-Me	*p*-Me	*p*-Ph	*m*-MeO	*p*-MeO
Concn. (g./l.)	1·6—1·9	1·7	1·0	0·20	0·78	1·1
λ (mμ)	335	335	325	335	345	350
X (in X·C_6H_4·CO·C_6H_5)	*m*-OH	*p*-OH	*p*-Br	*m*-NO_2	*p*-NO_2	
Concn. (g./l.)	0·82	0·046	1·6	0·46	0·094	
λ (mμ)	350	345	325	324	330	

THE UNIVERSITY, LEICESTER.

[*Received, March* 13*th*, 1959.]

609. *The Phenylation of Some Diazines.*

By C. M. ATKINSON and C. J. SHARPE.

Phenylations have been carried out with benzoyl peroxide, benzenediazonium salts, and *N*-nitrosoacetanilide. There is no evidence that phenylation of pyridazine has occurred at positions adjacent to the ring-nitrogen atoms. Quinoxaline yields 2-, 5-, and 6-phenylquinoxaline in the approximate ratio of 40 : 10 : 1. Phthalazine has given only 5-phenylphthalazine, but phenylation of cinnoline is more complex: 4 : 4′-dicinnolyl is the main product, 4-phenylcinnoline and an isomer have been isolated in much lower yield, and smaller amounts of four other products have been obtained.

PHENYLATION of nitrogen-heterocyclic compounds, by reactions involving free radicals, has received relatively little attention compared with the carbocyclic field. The results of the phenylation of pyridine, quinoline and benzothiazole have been summarised,[1] and further examination by Pausacker [2] of the phenylation of quinoline has shown the formation of 2 : 2′-diquinolyl as well as each of the monophenylquinolines; Hey and Walker [3] had already identified 4- and 5-phenylquinoline and indicated the presence of other products.

For the present work, pyridazine was prepared in excellent yield by a modification of a known method,[4] and quinoxaline was also readily available; [5] these compounds were used to select the most reliable and convenient phenylating agent for use with the less accessible heterocycles, cinnoline and phthalazine. The former has been prepared from methyl anthranilate in about 48% overall yield [6] and, in 22% overall yield, from *o*-aminoacetophenone *via* 4-hydroxycinnoline and 4-cinnolylhydrazine or its toluene-*p*-sulphonyl derivative.[7] However, reduction of 4-hydroxycinnoline with lithium aluminium hydride (*J.*, 1959, 2858) gave cinnoline in a yield of 52% (based on *o*-aminoacetophenone). Phthalazine was prepared by reduction of 1-chlorophthalazine with phosphorus and hydriodic acid (55% yield obtained; cf. 75% claimed [8]); lithium aluminium hydride reduction of tetra-*N*-methylphthalamide [9] was convenient only on the small scale. 1 : 4-Dichlorophthalazine,

[1] Dermer and Edmison, *Chem. Rev.*, 1957, **57**, 77.
[2] Pausacker, *Austral. J. Chem.*, 1958, 200.
[3] Hey and Walker, *J.*, 1948, 2213.
[4] Mizzoni and Spoerri, *J. Amer. Chem. Soc.*, 1951, **73**, 1873.
[5] Landquist, *J.*, 1953, 2817.
[6] Jacobs, Winstein, Henderson, and Spaeth, *J. Amer. Chem. Soc.*, 1946, **68**, 1310.
[7] Schofield and Swain, *J.*, 1950, 392; Alford and Schofield, *J.*, 1953, 609.
[8] Paul, *Ber.*, 1899, **32**, 2014.
[9] Weygand and Tietjen, *Ber.*, 1951, **84**, 625.

readily available[10] from the 1 : 4-dihydroxy-compound, gave with phosphorus and hydriodic acid about 35% of phthalazine, but variable amounts of 1-hydroxyphthalazine were also produced; reaction with toluene-*p*-sulphonhydrazide gave no useful product.

*Yield (%) * of phenylquinoxalines and 4-phenylpyridazine.*

Reagent	Quinoxalines			4-Phenyl-pyridazine
	2-Phenyl	5-Phenyl	6-Phenyl	
N-Nitrosoacetanilide	15·5	2·3	0·35	26 †
$PhN_2 \cdot OH$	1·9	0·45	0·05	2·3
Benzoyl peroxide	17·4	5·4	0·35	14
PhN_2Cl	0	0	0	7·2
$PhN_2 \cdot OAc$	0·4	0	0 ‡	

* Yields are based on the phenylating agent and on reaction (*a*) or (*b*), as appropriate:

(*a*) $Ph \cdot N_2X + RH \longrightarrow PhR + N_2 + HX$
(*b*) $(Ph \cdot CO \cdot O)_2 + RH \longrightarrow PhR + CO_2 + Ph \cdot CO_2H$

† A diphenylpyridazine (0·6%), m. p. 160—161°, was also isolated.
‡ 80% of the reagent was accounted for as *p*-hydroxyazobenzene or phenol.

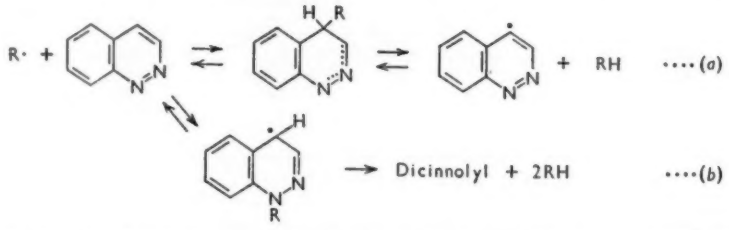
The annexed Table shows our phenylation results. If allowance is made for losses inherent in the separation of isomers by chromatography and fractional crystallisation, the isomer ratios are quite consistent. The trends are, in general, those which would be expected from consideration of the behaviour of pyridine and naphthalene towards free-radicals. Thus, in pyridine, the rate factors for phenylation at positions *o*-, *m*-, and *p*- to the ring-nitrogen atom are F_o (1·81), F_m (0·87), F_p (0·87),[11] while in naphthalene the additional fused ring results in greater activation than is conferred by any other substituent and phenylation gives α- and β-isomers in the ratio 5 : 1.[12] Benzoylation of some 1-substituted naphthalenes has revealed enhanced reactivity *para* to the substituent and the effects of the substituent and the fused ring are to some extent additive.[13] The isolation of 2-, 5-, and 6-phenylquinoxaline in an approximate ratio of 40 : 10 : 1, respectively, reflects the powerful activation of the ring-nitrogen atoms on the *ortho*-position, and the greater activity of the α- over the β-position in the *Bz*-ring. In the case of pyridazine, if the effect of two ring-nitrogen atoms may be calculated, from the pyridine data, by the method normally applied to two substituents in benzene,[14] then phenylation at $C_{(3)}$ in pyridazine should be more than twice that at $C_{(4)}$. In fact, no 3-phenylpyridazine was detected. The diphenylpyridazine, m. p. 160—161°, is probably the 4 : 5-compound since the 3 : 4-, 3 : 5-, and 3 : 6-isomers have been described[15] and the low concentration of 4-phenylpyridazine in the reaction precludes further phenylation to a diphenylyl derivative.

Only one pure compound (6% yield) was isolated from reaction between phthalazine and *N*-nitrosoacetanilide; this differed from 6-phenylphthalazine (*J.*, 1959, 2858), and from the 1-phenyl-isomer;[16] the compound, m. p. 174—175°, described as 1-phenylphthalazine[17] is probably dibenzaldazine;[18] our product is therefore represented as 5-phenylphthalazine. Since the majority of the products could not be separated, no conclusions can be drawn about the course of phenylation.

Phenylation of cinnoline with *N*-nitrosoacetanilide yielded a complex mixture: equal amounts of 4-phenylcinnoline and 5(or 8)-phenylcinnoline, were isolated. Fractionation of a mixture of picrates yielded another four products but in yields about one-tenth those

[10] Drew and Hatt, *J.*, 1937, 16.
[11] Hey *et al.*, *J.*, 1955, 3963; 1952, 2094.
[12] Huisgen and Sorge, *Annalen*, 1950, **566**, 162.
[13] Dannley and Gippin, *J. Amer. Chem. Soc.*, 1952, **74**, 332.
[14] Augood, Hey, and Williams, *J.*, 1953, 44.
[15] Almström, *Annalen*, 1913, **400**, 131; Paal and Schulze, *Ber.*, 1900, **33**, 3798, 3789.
[16] Liek, *Ber.*, 1905, **38**, 3922.
[17] Aggarwal, Darbari, and Ray, *J.*, 1929, 1941.
[18] Kochetkov and Varotnikova, *J. Gen. Chem.* (*U.S.S.R.*), 1956, **26**, 1927 (U.S. translation); Ikeda and Kanahara, *Ann. Rep. Fac. Pharm., Kanazawa Univ.*, 1955, **5**, 5.

of the monophenylcinnolines, which were insufficient to permit identification. The possibility of recycling the unchanged cinnoline to obtain more of these products could not be realised since each run yielded ten times as much 4 : 4′-dicinnolyl as all the other products combined. Thus it appears that substitution is more difficult to achieve than hydrogen-abstraction from $C_{(4)}$. Two mechanisms (*a*) and (*b*), for this process are possible.



The mechanism involving the σ-complex (*a*) has been discussed by Augood and Williams [19] and is supported by the isolation of methane on reaction of toluene with atomic hydrogen.[20] The alternative (*b*), involving a quinonoid intermediate, is similar to that postulated for the formation of diaryls in the reaction between chlorobenzene and methyl [21] or phenyl [14] radicals. The ready formation of dicinnolyl is reminiscent of its formation, as the major product, on catalytic hydrogenation of 4-chlorocinnoline, and, as the minor product on decarboxylation of cinnoline-4-carboxylic acid: [22] although the latter formation has been regarded as arising from a protonised cinnolyl anion the obvious activity of a cinnolyl free-radical supports the possibility of decarboxylation by a free-radical mechanism. Comment on the phenylated derivatives must await identification of the four minor components, but at least one of these must be an anomalous product.

Experimental

Light petroleum had b. p. 40—60° unless otherwise stated. Solvents used for chromatography were dried (over sodium where possible) and redistilled.

Pyridazine.—3 : 6-Dichloropyridazine (29·6 g.), alcohol (70 ml.), aqueous ammonia (*d* 0·880; 32 ml.), and 5% palladised charcoal (2 g.) were shaken with hydrogen at 3—5 atm. for 65 min., then combined with two other batches (from 29·6 and 30·1 g. of dichloropyridazine) and filtered, and the catalyst was washed with benzene (200 ml.). The filtrate and washings were evaporated, and the residual benzene solution was made up to 600 ml. with benzene, and dried azeotropically (Dean and Stark apparatus). The solution was cooled, shaken with solid potassium hydroxide, and filtered from inorganic material. The filtrate was first evaporated to 100 ml. under slightly reduced pressure, the last traces of solvent being removed at 1 mm. (it is important that air should not be admitted to the apparatus at this stage as the crude pyridazine is liable to inflame); pyridazine distilled as a very pale yellow liquid (42·6 g., 89%), b. p. 50—51°/1 mm.

Phthalazine.—(*a*) 1-Chlorophthalazine (18 g.) and toluene-*p*-sulphonhydrazide (42 g.) were heated under reflux in dry chloroform (420 ml.) for 2 hr. The product (30·2 g.), m. p. 217° (decomp.), was collected when cold, washed with a little chloroform and then with light petroleum, and dried in air. Trituration with acetone and recrystallisation from glacial acetic acid gave 1-N′-(*toluene*-p-*sulphonyl*)*hydrazinophthalazine hydrochloride*, m. p. 220° (decomp.) (Found: C, 51·7; H, 5·0; N, 15·3; Cl, 11·4. $C_{15}H_{15}O_2N_4SCl$ requires C, 51·4; H, 4·3; N, 15·9; Cl, 10·1%). The crude salt (30·2 g.) was added portionwise during 1 hr. to N-sodium hydroxide (435 ml.) at 90—95° with stirring and heated on the water-bath for a further 1 hr. Continuous extraction with benzene provided phthalazine (7·8 g., 55%) as a pale yellow solid, m. p. 89—91° (lit., 91°).

[19] Augood and Williams, *Chem. Reviews*, 1957, **57**, 123.
[20] Szwarc, *Nature*, 1948, **161**, 890.
[21] Beckwith and Waters, *J.*, 1957, 1665.
[22] Morley, *J.*, 1951, 1971.

(*b*) 1 : 4-Dichlorophthalazine (10 g.), red phosphorus (5 g.), and hydriodic acid (*d* 1·7; 165 ml.) were heated under reflux for 80 min. The solution was diluted with water (150 ml.), cooled, filtered, made alkaline with concentrated potassium hydroxide solution, and extracted continuously with benzene. On concentration of the extract to 50 ml., 1-hydroxyphthalazine (1·0 g.), m. p. 183—184°, separated, and complete removal of solvent from the mother-liquors yielded phthalazine (1·95 g., 35%), m. p. 90—91°, b. p. 134°/1·5 mm.

The potassium hydroxide solution was evaporated to dryness on the water-bath, and the residue boiled with chloroform (750 ml.) and filtered. The residue after evaporation of the filtrate was dissolved in 3N-sodium hydroxide from which 1-hydroxyphthalazine (3 g.), m. p. 183—184°, was precipitated on acidification.

Phenylation of Quinoxaline.—The phenylquinoxalines and their picrates were identified by mixed-melting-point determinations with authentic samples.

(a) *With* N-*nitrosoacetanilide.* *N*-Nitrosoacetanilide (8·2 g., 0·05 mole) was added portionwise during 1 hr. to stirred molten quinoxaline (75 g., 0·5 mole) at 38—40° and the mixture was stirred at 40° until gas evolution ceased (3 hr.). Ether (*ca.* 250 ml.) was added and the solution was extracted with 3N-sodium hydroxide (150 ml. in all). The washed and dried ($MgSO_4$) ether layer was evaporated, finally under reduced pressure, and the excess of quinoxaline was recovered by distillation at 70—75°/2—3 mm. A further small quantity of quinoxaline was recovered as its picrate (m. p. 160—161°) from methanol washings of the apparatus (total recovery, 63·1 g.).

Eluant * (ml.)	Recryst. from *	Quinoxaline	Product Wt. (g.)	M. p.
Table A				
Pet (400)	Pet	2-Ph	0·8	78°
1 : 1-C_6H_6–Pet (400)	Pet, aq. MeOH	2-Ph	0·41	78
C_6H_6 (160)	Pet	2-Ph †	<0·01	98—101
1 : 3-$CHCl_3$–C_6H_6 (280)	—	†	—	—
MeOH–Et_2O	—	Tar	—	—
Table B				
Pet (200)	—	2-Ph	0·36	78
	—	Picrate	0·06	122
1 : 2-C_6H_6–Pet (200)	—	5-Ph	0·1	124
2 : 1- ,, (200)	—	Picrate	0·08	148
C_6H_6 (200)	—	6-Ph picrate	0·07	170

* Pet = light petroleum (b. p. 40—60°). † Impure.

The residue in the distillation flask was digested with warm 5N-hydrochloric acid (150 ml.) and filtered from a black solid (3·2 g.), m. p. 230°. The acid extract was made alkaline with concentrated aqueous potassium hydroxide and extracted with ether. Some black intractable tar, which was sparingly soluble in ether, was rejected. The basic fraction (7·6 g.), a brown oil obtained by evaporation of the dried ($MgSO_4$) ether-extract, was transferred in benzene (40 ml.)–light petroleum (10 ml.) to a column of alumina (100 g., type H). Table A shows the fractionation thus achieved. The crystallisation mother-liquors from these fractions were combined, evaporated, and chromatographed again on alumina (35 g.) with the results shown in Table B.

(b) *With benzenediazohydroxide.* Aniline (9·3 g.) in concentrated hydrochloric acid (35 ml.) and water (10 ml.) was diazotised at 0—5° with sodium nitrite (7·1 g.) in water (30 ml.). Quinoxaline (78 g.) was added and the mixture was stirred at 0—5° during the addition, in 1½ hr., of sodium hydroxide (16 g.) in water (60 ml.), and then for a further 1 hr. After being stirred overnight at room temperature, the solution was made strongly alkaline with 6N-sodium hydroxide and extracted with ether. The dried ($MgSO_4$) extract yielded, by distillation, quinoxaline (68·4 g.), b. p. 70—75°/2—3 mm. The high-boiling residues from three such experiments were taken up in ether and extracted with 5N-hydrochloric acid, and the extract was washed with ether, made alkaline with 6N-sodium hydroxide, and extracted with ether. The basic fraction so obtained, a dark brown oil (8·2 g.), was separated as in (a).

(c) *With benzenediazonium chloride.* Aniline (2 g.) in concentrated hydrochloric acid (3·8 ml.) and water (1 ml.) was diazotised in the usual way and added during 1 hr. to quinoxaline (28 g.) stirred at 40°. Stirring was continued for ½ hr. (no further gas evolution) and the mixture was treated as in (b). Apart from quinoxaline (92%) and phenol, no recognisable product was obtained.

(d) *With benzenediazonium acetate.* Aniline (4·65 g.) in concentrated hydrochloric acid (17·5 ml.) and water (5 ml.) was diazotised as usual, and powdered quinoxaline (36 g.) was added. The mixture was stirred at 0° ± 2° during the addition, in 1 hr., of aqueous sodium acetate (8 g. in 20 ml.), and for another 2 hr.; stirring was continued at room temperature for for 24 hr. (no further gas evolution). Isolation as in (b) yielded 4-hydroxyazobenzene (2·9 g.), phenol (0·9 g.), 2-phenylquinoxaline picrate (0·09 g.), and quinoxaline (95%).

(e) *With dibenzoyl peroxide.* A mixture of quinoxaline (78·2 g.) and dry dibenzoyl peroxide (12·1 g.) was stirred at 80—85° for 72 hr. Separation by the method employed in (b) gave an acidic fraction which consisted of benzoic acid (6·93 g.) and a brown oil (1·15 g.) which resisted attempts at purification. The basic fraction yielded quinoxaline (61·9 g.), three monophenylquinoxalines, a small quantity of a mixture, m. p. 180—280°, and residual tar.

Phenylation of Pyridazine.—4-Phenylpyridazine (m. p. 86°) and its picrate (m. p. 166°) were identified by mixed m. p. determinations.

(a) *With N-nitrosoacetanilide.* Pyridazine (40 g.) was stirred at 40—45° during the portionwise addition, in 1½ hr., of *N*-nitrosoacetanilide (8·2 g.). The cold-water bath was removed and the temperature was kept at 40° for a further ½ hr. Distillation at 48—50°/0·8 mm. gave pyridazine contaminated with some acetic acid (39 g., *i.e.*, a minimum recovery of 36 g. of pyridazine).

The residue in the distillation flask was digested with hot 5N-hydrochloric acid, filtered, cooled, and made alkaline with solid potassium hydroxide. Extraction with benzene yielded a brown sticky solid (4·1 g.), unchanged by chromatography on an alumina column. This fraction was distilled through a 5″ column and yielded a yellow solid (2·72 g.), m. p. 74—84°, b. p. 100—120°/0·1—0·5 mm., from which 4-phenylpyridazine (1·82 g.) was obtained by recrystallisation from ligroin. The mother-liquors gave a residue which was converted into 4-phenylpyridazine picrate (0·24 g.). The remaining distillate (0·71 g.), b. p. 120°/0·1 mm., was a yellow oil from which, by recrystallisation from ligroin, then digestion with hot water, there was obtained a colourless product, presumably, 4 : 5-diphenylpyridazine (65 mg.), m. p. 160—161°. This gave a picrate which crystallised as yellow needles, m. p. 193°, from methanol or aqueous ethanol (Found: C, 57·4; H, 3·2; N, 15·2. $C_{22}H_{15}O_7N_5$ requires C, 57·25; H, 3·3; N, 15·2%). The ligroin and aqueous mother-liquors, on evaporation, gave a further 0·25 g. of 4-phenylpyridazine picrate.

(b) *With benzenediazohydroxide.* A diazotised solution of aniline (9·3 g.) was cooled to −10°, pyridazine (42·4 g.) was added, and the mixture stirred at −10° to −5° during addition, in 1½ hr., of a concentrated solution of sodium hydroxide. After a further 2 hr., the cooling-bath was removed and stirring was continued overnight. The mixture was acidified with concentrated hydrochloric acid, and after ½ hour's stirring the black tar (2·9 g.) which remained undissolved was removed. No pure compound could be obtained from the tar by chromatography on alumina.

The acid solution was washed with ether from which phenol (0·4 g.) was obtained, and the cooled aqueous layer was made alkaline with solid potassium hydroxide. Tar (2·5 g.) was removed, and the solution was concentrated *in vacuo* over sodium hydroxide, the last traces of water being removed by azeotropic distillation with benzene. Inorganic material was filtered from the benzene solution (250 ml.) and was washed with benzene, and the filtrate was distilled, finally under reduced pressure. The fraction of b. p. 74—78°/4 mm. was redistilled to yield pyridazine (27·4 g.), b. p. 78°/5 mm. The residue in the distillation flask yielded on digestion with ether an oily, brown solid (4·4 g.), which was chromatographed in benzene (15 ml.) and light petroleum (b. p. 40—60°; 5 ml.) on alumina (60 g., type H) with elution with benzene (400 ml.). Evaporation of the eluate and successive recrystallisation of the residue from light petroleum (b. p. 80—100°) and water yielded 4-phenylpyridazine (0·36 g.), m. p. 86·5°. The residues from the mother-liquors, on treatment with methanolic picric acid, gave only 4-phenylpyridazine picrate.

(c) *With benzenediazonium chloride.* Aniline (2 g.) was diazotised as usual and the solution was added dropwise, during 1 hr. with stirring, to pyridazine (20 g.), at 40°. After a further 45 min., the solution was cooled, made alkaline with 6N-potassium hydroxide, mixed with benzene, and dried azeotropically; after removal of inorganic material, the benzene solution was evaporated, finally under reduced pressure. Pyridazine was distilled from the residue and redistilled (16·1 g.; b. p. 78°/5 mm.); pyridazine picrate (2·8 g.; m. p. 172°) was obtained from mother-liquors and washings. A solution of the high-boiling residue in benzene

(250 ml.) was extracted with 5N-hydrochloric acid (4 × 55 ml.), washed with water, and, on evaporation, yielded only phenol (0·3 g.). The basic fraction (1·2 g.), a brown, sticky solid obtained by the procedure used in (a), yielded on distillation through a 5″ column a white solid (0·76 g.), m. p. 58—72°, b. p. 130—160°/1—2 mm. Three recrystallisations from light petroleum (b. p. 80—100°) gave 4-phenylpyridazine (0·24 g.), m. p. 80—83°, and the mother-liquors, yielded a mixture of picrates (140 mg.), m. p. 120—155°, which could not be separated.

(d) *With dibenzoyl peroxide.* Dry dibenzoyl peroxide (11·1 g.) was dissolved in pyridazine (35·9 g.) and warmed gently. At 30° a vigorous reaction set in, and the temperature rose rapidly to 180° despite water-cooling. The dark solution was stirred at 40° for 1 hr., then worked up as (a). Pyridazine (28 g.) was recovered and the less volatile distillate (1·08 g.), b. p. 100—130°/0·5 mm., gave 4-phenylpyridazine (1·01 g.), m. p. 86°, by recrystallisation from ligroin.

Phenylation of Phthalazine.—Phthalazine (26 g.; m. p. 91°) was stirred at 95—100° and this temperature was maintained initially by portionwise addition of *N*-nitrosoacetanilide (3·3 g.) in 30 min., and later, for 2 hr., by external heating. Distillation yielded phthalazine (20·2 g.), m. p. 89—91°, b. p. 112°/0·5 mm., and acetic acid (collected in a trap at about −40°), but no detectable quantity of benzene. Cold-water washing of the high-boiling residue provided phthalazine (2·3 g.). The water-insoluble residue was warmed with benzene (300 ml.), filtered from insoluble tar, and extracted with 6N-hydrochloric acid (5 × 30 ml.). The benzene solution yielded a brown oil (0·45 g.), from which no pure compound could be obtained. The aqueous solution was made alkaline with 6N-potassium hydroxide and extracted with chloroform, to provide a basic fraction (2·7 g.) which was transferred in benzene (10 ml.) to a column of alumina (27 g.; type H). Fractions obtained by elution with light petroleum and benzene–light petroleum were yellow or brown oils or sticky solids; these crystallised with difficulty from ligroin, giving the same yellow solid, m. p. 100—106°. Sublimation of the crude solid at 130°/0·5 mm. gave 5-*phenylphthalazine* (0·33 g.), m. p. 104—106°, which crystallised in colourless plates, m. p. 106°, from ligroin (Found: C, 81·6; H, 5·15; N, 13·45. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·6%). Further elution of the column with benzene and with 1 : 1 chloroform–benzene gave dark oils which yielded no identifiable products.

Phenylation of Cinnoline.—Cinnoline (45 g.) was stirred at 55—60° during portionwise addition of *N*-nitrosoacetanilide (5·7 g.) during 50 min. Stirring was continued at 60° for 2 hr. and the mixture was distilled, a fraction of b. p. 124—126°/1 mm. being collected. This distillate was dissolved in benzene, treated with anhydrous sodium carbonate, filtered, and evaporated. The resultant green solid (42 g.), m. p. 30°, was distilled to yield yellow material (38·8 g.), m. p. 35°, b. p. 124°/1 mm.; residues and washings yielded cinnoline picrate (4·6 g.), m. p. 196°.

The fraction of b. p. 124°/1 mm. was digested with water (850 ml.) on the steam-bath for ¾ hr., and the insoluble portion (6·75 g.), m. p. 144—186°, was collected from the cooled mixture, washed with water, and dried *in vacuo*. This product (5·1 g.) was recrystallised from alcohol, and, after filtration from a less-soluble orange residue (0·7 g.), m. p. 210—225°, gave yellow needles (4·0 g.), m. p. 232—237°. Further recrystallisation from methanol and benzene gave yellow needles of 4 : 4′-dicinnolyl, m. p. and mixed m. p. 238° (Found: C, 74·7; H, 4·0; N, 21·5. Calc. for $C_{16}H_{10}N_4$: C, 74·5; H, 3·9; N, 21·7%).

The residue from the original distillation was extracted with 5N-hydrochloric acid (3 × 40 ml.), and the extract was filtered and washed with ether (the ether washings contained only a small quantity of tar). The aqueous layer was made alkaline with 6N-sodium hydroxide and extracted with benzene to yield the basic fraction (4·0 g.), a brown oil, which was transferred in benzene (10 ml.) and light petroleum (5 ml.) to alumina (40 g.; type H). Elution with light petroleum gave oils, which were converted into picrates and yielded, after several recrystallisations from water and dilute methanol, 4-phenylcinnoline picrate (0·43 g.), m. p. and mixed m. p. 158°, and another picrate (130 mg.), m. p. 138—140°. The remaining picrates could not be separated and were decomposed by hot 3N-sodium hydroxide from which chloroform-extraction yielded a green oil.

Elution with benzene–light petroleum gave oils which, after several recrystallisations from light petroleum (b. p. 60—80° and b. p. 80—100°) and from ligroin, gave pale yellow plates of a *phenylcinnoline* (0·45 g.), m. p. 131° (Found: C, 80·5; H, 5·2; N, 14·7. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·6%). The picrate of this compound crystallised from benzene in deep yellow plates, m. p. 208°.

Elution with benzene and with 1 : 1 benzene–chloroform gave oils; these were chromatographed again on alumina. Residues from mother-liquors and from decomposed picrates were rechromatographed separately. Some of the residual oils gave picrates, fractional crystallisation of which gave yellow solids (50 mg.), having m. p.s 158°, 172°, and 154° severally. These were distinguished from one another and from 4-phenylcinnoline picrate by mixed-m. p. determinations.

The authors are indebted to Messrs. Albright and Wilson Ltd. for a grant (to C. J. S.).

CHEMISTRY DEPARTMENT, CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W.3.
DERBY AND DISTRICT COLLEGE OF TECHNOLOGY. [*Received, December 5th*, 1958.]

---

610. *Synthetical Applications of Activated Metal Catalysts. Part VII.* The Formation of 2,2′-Bipyridyl and 2-2′-Pyrrolylpyridine from Pyridine under the Influence of Degassed Raney Nickel.*

By W. H. F. SASSE.

A modified Raney nickel catalyst is described. Its action on pyridine under varied conditions is reported.

THE preparation of 2,2′-bipyridyl from pyridine by means of degassed Raney nickel [1] is complicated by the formation of a nickel(II) complex which contains 2,2′-bipyridyl and 2,2′-pyrrolylpyridine.[2] I now report some of the factors which influence the yields of these products. During this work it became necessary to alter the method of preparation of the catalyst as explosions occurred repeatedly during the degassing of the Raney

Reaction between W7-J *Raney Nickel Catalyst and Pyridine.*

No.	Time (hr.)	Pyridine (c.c.)	2,2′-Bipyridyl [a] (g.)	Complex [b] (g.)	Ratio [c]
1	6	250	12	0·3	2·5
2	11	250	20	0·5	2·5
3	21	250	27·5	1·2	4·4
4	46	250	30	1·5	5
5	70	250	30·5	1·8	5·9
6	187	250	30	4·0	7·5
7 [d]	46	250	26	2·5	9·6
8 [d]	53	225	3	0·8	37·5
9 [d]	49	250	22	2·0	9·1
10	22	89	18	1·7	9·5
11 [e]	28	89	3·2	0·38	11·9
12 [e]	27	89	3·6	0·44	12·2
13 [e]	27	42	1·5	0·5	33·3
14 [f]	44	250	26	2·5	9·6
15 [d,f]	46	250	4	0·005	0·125
16 [g]	—	150	5	0·04	0·8
17 [g]	—	150	16	0·8	5

Yields refer to about 1 g.-atom of nickel (prepared from 125 g. of 50 : 50 aluminium–nickel alloy). [a] After chromatographic purification. [b] After washing with boiling light petroleum, b. p. 60—90°; dried *in vacuo*. [c] 100 × Weight of complex/Weight of 2,2′-bipyridyl. [d] Experiment with pyridine containing pyrrole. [e] Experiment with pyridine diluted with mesitylene. [f] Experiment in the presence of nickel(II) acetate. [g] Experiment by passing pyridine through a column packed with the catalyst.

nickel.[3] With the modified catalyst, named W7-J Raney nickel, the dimerisation of pyridine ceased after about 2 days, while the formation of the complex continued at an approximately constant rate for at least a week (see Table, Nos. 1—6). In the presence of a solvent the yields of both products were lower (compare No. 10 with Nos. 11, 12), but

* Part VI, *J.*, 1959, 440.

[1] Badger and Sasse, *J.*, 1956, 616.
[2] Sargeson and Sasse, *Proc. Chem. Soc.*, 1958, 150.
[3] Cf. Smith, Chadwell, and Kirslis, *J. Phys. Chem.*, 1955, **59**, 820.

the amount of complex formed relative to that of 2,2′-bipyridyl was slightly increased. A large proportion of nickel had a similar effect (Nos. 3, 10), particularly when the reaction was carried out in a solvent (Nos. 12, 13). The addition of either pyrrole (Nos. 7, 9) or nickel(II) acetate (No. 14) interfered with the dimerisation (cf. No. 4), and the yield of complex increased. Larger amounts of pyrrole (10%) (No. 8), or simultaneous addition of pyrrole and nickel(II) acetate, led to very much reduced yields of both products (No. 15). When the reaction was carried out by passing pyridine through a column packed with the catalyst, at 60—70°, the yield of the complex was more sensitive to changes in the rate of flow of the pyridine than was the formation of 2,2′-bipyridyl, and at higher rates of flow the dimerisation of pyridine could be carried out with a minimum of side reactions.

Traces of pyrrole were detected in the reaction mixture (see below), but no attempts were made to identify other pyrroles which may have been present in smaller amounts. The results obtained with W7-J Raney nickel show that the pyrrole which is formed in the reaction between the catalyst and pyridine interferes with the formation of 2,2′-bipyridyl, and as the addition of small quantities of pyrrole increases the yield of the complex (Nos. 7, 9), it seems likely that the 2,2′-pyrrolylpyridine is derived from a reaction involving pyrrole. The formation of pyrrole from pyridine under the conditions used in the present work is of interest, as earlier examples of the formation of pyrroles from pyridines during hydrogenations over nickel catalysts were observed at much higher temperatures.[4]

A Raney nickel catalyst which had been washed free from alkali gave the complex and 2,2′-bipyridyl in reduced yields, but in the same ratio as did the W7-J Raney nickel catalyst. When W7 Raney nickel was used no complex could be detected, and much less 2,2′-bipyridyl was isolated. However, colour tests indicated the presence of traces of pyrroles.

Experimental

Preparation of W7-J *Nickel Catalyst.*—Explosions occurred on several occasions during the degassing of the catalyst which had been prepared as described previously [1] from an aluminium–nickel alloy (50 : 50) with an average particle size of 4μ (as determined with a Fisher subsieve sizer). However, this procedure could be safely used when seven non-return valves (of the type used in bicycle tubes) were incorporated in the vacuum-line close to the flask containing the nickel. Alternatively, the same alloy was satisfactory when the following modifications were adopted: The alloy was added to the aqueous solution of sodium hydroxide as described, but without external cooling. Then the catalyst was digested for 6 hr. at 100° while being gently stirred. After being kept at room temperature overnight, the nickel was washed and transferred to a three-necked round-bottomed flask (500 c.c.) equipped with a dropping funnel. This flask was connected to two 3-l. Buchner flasks which in turn were connected to two efficient water-pumps. All connections were made with short pieces of stout, large-bore rubber tubing (int. diam. 9 mm.; ext. diam. 15 mm.). After evacuation of the apparatus at room temperature, the flask containing the catalyst was slowly warmed so as to avoid losses of the nickel by vigorous boiling. After being kept at 100°/15—20 mm. for about 2 hr. the catalyst was ready for use. Pyridine was added through the dropping funnel to the cooled catalyst as previously described.

An aluminium–nickel alloy with an average particle size of 2·85 μ invariably lost hydrogen in an explosive fashion at about 80°/15—20 mm., but could be degassed with the use of non-return valves.

Purification of Pyridine.—Pyridine was fractionated through the column described before,[5] with a reflux ratio 1 : 10. When the b. p. reached 115°, anhydrous potassium hydroxide (10 g./100 c.c. of pyridine) was added. After 2 hours' heating under total reflux, fractionation (reflux ratio 1 : 10) was continued. Pyridine containing between 0·001 and 0·0001 vol.-% of pyrrole did not react with *p*-dimethylaminobenzaldehyde after this treatment. When higher concentrations of pyrrole were present the fractionation had to be repeated.

[4] Padoa, *Gazzetta*, 1908, **38**, 228; Granelli, *Farm. Ital.*, 1937, **5**, 708; Jones, *J.*, 1950, 1392; Jones and Lindsey, *J.*, 1952, 3261.
[5] Badger, Rodda, and Sasse, *J.*, 1954, 4162.

Pyridine and W7-J *Nickel Catalyst.*—With the exception of two experiments (see Table, Nos. 16, 17) all reactions were carried out by refluxing pyridine over the catalyst (in every case prepared from 125 g. of 50 : 50 aluminium–nickel alloy). The products were isolated in the way described,[1] and the results are summarised in the Table. The following experiments were carried out with pyridine in the presence of other compounds.

No. 7. Pyrrole was added in four portions (1 c.c. each) at intervals of 9 hr., beginning 15 min. after the reaction had been started with pyridine (250 c.c.).

No. 8. Pyrrole (25 c.c.) in pyridine (225 c.c.) was used.

No. 9. Pyridine (250 c.c.; b. p. 115°), recovered from experiment No. 3 by distillation, was used.

No. 11. Pyridine (89 c.c.) and mesitylene (89 c.c.) were used.

No. 12. Pyridine (89 c.c.) and mesitylene (267 c.c.) were used.

No. 13. Pyridine (42 c.c.) and mesitylene (126 c.c.) were used.

No. 14. A solution of nickel(II) acetate (3 g.) in pyridine (30 c.c.) was added in portions (10 c.c.) at intervals of 12 hr., beginning 1 hr. after reaction had been started with pyridine (250 c.c.).

No. 15. Pyrrole (1 c.c.) was added 1 hr. after reaction had been started with pyridine (250 c.c.). One hr. later, nickel(II) acetate (1 g.) in pyridine (10 c.c.) was added.

No. 16. After having been degassed, the catalyst was wetted with pyridine (100 c.c.) and packed into a column (ext. diam. 2 cm.), placed in a heating jacket, and the temperature kept at 60—70° while pyridine (150 c.c./hr.) was passed through it for 1 hr.

No. 17. The apparatus and conditions of experiment No. 16 were used, except for a rate of flow of 50 c.c./hr. of pyridine for 3 hr.

Detection of Pyrrole in Pyridine.—(*a*) Pyridine (0·1 c.c.) was diluted with water (0·5 c.c.). Concentrated hydrochloric acid (0·5 c.c.) was added, followed by a 5% solution (0·1 c.c.) of *p*-dimethylaminobenzaldehyde in aqueous 1·3N-hydrochloric acid.[6] In the presence of pyrrole a purple-red colour was produced (lower limit 0·0001 vol.-% of pyrrole in pyridine).

(*b*) Other reagents which were used for the detection of pyrrole included: isatin and concentrated sulphuric acid [7] (deep blue colour; lower limit 0·01 vol.-%); selenium dioxide and concentrated nitric acid [7] (deep purple colour; lower limit 0·1 vol.-%); phenyldiazonium chloride and aqueous sodium carbonate solution [8] (bright red precipitate; lower limit 0·01 vol.-%).

(*c*) Detection of pyrrole in pyridine by paper chromatography was difficult because of the volatility of the mixture. However, by the addition of picric acid to the spots of the mixture on Whatman paper No. 1 the picrates of the components were produced which were then developed by ascent with 2% aqueous acetic acid. The picrate of pyridine streaked, probably because of partial dissociation (R_F 0·23—0·81). The picrate of pyrrole dissociated readily to give picric acid (R_F 0·81) and pyrrole (R_F 0·95). The latter was made visible by exposure of the paper to iodine vapour.

(*d*) Gas–liquid partition chromatography was used for the identification and estimation of pyrrole. A Griffin V.P.C. apparatus Mk II was used with a four ft. column packed with Celite (40—80 mesh; 20% Apiezon L). At 150° the retention times observed were for pyridine, 2·18 min., and for pyrrole, 1·71 min. (outlet pressure 139 mm.; inlet pressure 333 mm.; flow rate 1·4 l./hr. of nitrogen; bridge current 133 milliamp.). From the peak areas the approximate composition of the mixture could be measured.

(*e*) As described by Densham, Langston, and Gough,[9] examination of the infrared spectra of mixtures of pyridine and pyrrole in the region 9—10 μ gave results comparable with those obtained by gas-phase chromatography.

Detection of Pyrrole in the Reaction between Pyridine and W7-J *Nickel.*—Pyrrole was detected in each experiment which was conducted with pyrrole-free pyridine (see Table, Nos. 1—6, 10—14) within 5—8 min. from the beginning of refluxing, by means of *p*-dimethylaminobenzaldehyde. After 24 hr. (Nos. 4—6, 10—14) all other tests described confirmed the presence of pyrrole. Gas–liquid chromatography and infrared spectra showed the presence of pyrrole

[6] Fischer and Nenitzescu, *Z. physiol. Chem.*, 1925, **145**, 295.
[7] Fischer and Orth, "Die Chemie des Pyrrols," Vol. I, p. 25, Akademische Verlagsgesellschaft, Leipzig, 1934.
[8] Fischer and Hepp, *Ber.*, 1886, **19**, 2251.
[9] Densham, Langston, and Gough, *J.*, 1952, 2433.

after refluxing had been continued for 5 days (No. 6). After one week part of the pyridine (No. 6) was removed by filtration without dilution with fresh pyridine; after distillation from a water-bath at 20 mm. (to remove complex and 2,2′-bipyridyl), it contained 1 ± 0·2 vol.-% as determined by the last-mentioned methods (checked against standard mixtures).

Nos. 16, 17. When the temperature of the column had reached 60° pyrrole was detected by means of *p*-dimethylaminobenzaldehyde in the pyridine which had been passed through the column.

Experiments with Other Raney Nickel Catalysts.—The conditions of experiment No. 4 (see Table) were used throughout.

(*a*) Neutral degassed Raney nickel was prepared by adding the alloy to the aqueous solution of sodium hydroxide in the usual way. The catalyst was then washed with distilled water (about 10 l.) until the washings were neutral and degassed as described above. This catalyst gave 2,2′-bipyridyl (24 g.) and complex (1·25 g.), equal to 5·2% of the weight of 2,2′-bipyridyl obtained.

(*b*) W7 Raney nickel [10] was freed from water with methanol and three times washed by decantation with pyridine (3 × 75 c.c.). 2,2′-Bipyridyl (3·6 g.) was obtained but no complex was isolated. Pyrrole was detected in the recovered pyridine by means of *p*-dimethylaminobenzaldehyde.

The author thanks Professor G. M. Badger for his interest in this work, and Dr. H. J. Rodda and Mr. A. G. Moritz for infrared spectra.

THE UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, December 17th*, 1958.]

[10] Billica and Adkins, *Org. Synth.*, 1949, **29**, 24.

---

611. *The Formation of Hydrocarbon Positive Ions in Strong Proton Donors.*

By W. Ij AALBERSBERG, G. J. HOIJTINK, E. L. MACKOR, and W. P. WEIJLAND.

The electronic spectra were measured of solutions of highly basic aromatic hydrocarbons in concentrated sulphuric acid, in oxygenated anhydrous hydrogen fluoride, and in oxygenated mixtures of trifluoroacetic acid and BF_3,H_2O. In the last, the spectra of solutions of perylene, tetracene, pyrene, anthracene and 3,4-benzopyrene resemble those of the corresponding mononegative ions. Similar observations were made with solutions of perylene, tetracene, and anthracene in the other solvents. We conclude that under these conditions the monopositive ions of these hydrocarbons are formed by electron transfer.

The solutions of anthracene in sulphuric acid as well as in hydrogen fluoride in the presence of oxygen display the spectra of the proton complex and of the anthracene monopositive ion. 3,4-Benzopyrene forms only proton complexes in these acids.

This difference in behaviour is discussed on the basis of the relative stabilities of monopositive ion and proton complex calculated from their oxidation potentials and basicity constants.

YOKOZAWA and MIYASHITA [1] discovered that a solution of perylene in concentrated sulphuric acid is paramagnetic. Weissman, de Boer, and Conradi [2] found that its electron spin resonance spectrum is nearly identical with the characteristic spectrum of the perylene mononegative ion. The electronic absorption spectra of perylene in sulphuric acid and its mononegative ion are also strikingly similar.[3] In the light of current quantum-chemical

[1] Yokozawa and Miyashita, *J. Chem. Phys.*, 1956, **25**, 796.
[2] Weissman, de Boer, and Conradi, *J. Chem. Phys.*, 1957, **26**, 963; de Boer and Weissman, *J. Amer. Chem. Soc.*, 1958, **80**, 4549; de Boer, Thesis, Free University, Amsterdam, 1957.
[3] Hoijtink and Weijland, *Rec. Trav. chim.*, 1957, **76**, 836.

XUM

theories these and other experimental results point to the formation of the perylene monopositive ion.[2,3,4] Gold and Tye,[5] on the other hand, demonstrated that anthracene in sulphuric acid forms a proton complex. Apparently, when aromatic hydrocarbons dissolve in strongly proton-active and oxidizing media both proton complexes and positive ions may be formed. This is confirmed by recent investigations on perylene in anhydrous hydrogen fluoride.[6] In absence of oxygen, perylene dissolves in the acid as the proton complex. When the solutions come into contact with oxygen, however, the absorption bands of the proton complex become very weak and a spectrum appears which closely resembles that of perylene in sulphuric acid.

The absorption spectra [42—10 kK (K, Kaiser ≡ cm.$^{-1}$)] of strongly basic aromatic hydrocarbons dissolved in concentrated sulphuric acid as well as in anhydrous hydrogen fluoride and a mixture of trifluoroacetic acid and BF_3,H_2O containing oxygen have been measured. On the basis of the results the relative stabilities of monopositive ions and proton complexes in strong proton donors with oxidizing properties are discussed.

Experimental

Hydrocarbons in Sulphuric Acid (with R. van Hardeveld and J. van der Ree).—In the preparation of the solutions of aromatic hydrocarbons in sulphuric acid (" AnalaR " 96%) no special precautions were taken to exclude air and moisture. The hydrocarbons were from the same source as previously.[7,8]

The spectra were measured on a Unicam SP.500 spectrophotometer. Solutions of perylene and tetracene ($0{\cdot}01$—$0{\cdot}5 \times 10^{-4}$M) obeyed the Beer–Lambert law.

Hydrocarbons in Anhydrous Hydrogen Fluoride and in Mixtures of Trifluoroacetic Acid with BF_3,H_2O.—Carefully purified samples of the hydrocarbons were used.[8]

The equipment for use with hydrogen fluoride was made of monel and nickel. It comprised a vessel with calibrated Kel-F windows, and the absorption cell, which has been described elsewhere,[6] mounted together on a panel. A weighed amount of hydrocarbon was placed in the calibrated vessel and hydrogen fluoride (I.C.I., pure grade) was distilled in *in vacuo*. By rotating the panel the solution was made to flow into the evacuated cell, which had a variable thickness ($0{\cdot}2$—2 mm.). The cell was detached from the assembly, and the spectrum measured. Oxygen could be introduced into the system at pressures of up to 3 atm.

No special precautions were taken in handling the solutions in mixtures of CF_3CO_3H–BF_3,H_2O, since they do not attack either quartz or Pyrex. The solvent was prepared by saturating trifluoroacetic acid (Matheson Inc., redistilled) containing 22 moles % of water with boron trifluoride (Fluka AG; carefully fractionated) at atmospheric pressure. Finally, the solutions of the hydrocarbons in $CF_3{\cdot}CO_3H$–BF_3,H_2O were saturated with air.

The spectra were measured on a Cary spectrophotometer, model 11 or 14 (thermostatted at 25°).

Results.—The results obtained with perylene, tetracene, anthracene, 3,4-benzopyrene, and pyrene are in Figs. 1—5. Our remarks apply to the individual observations.

For comparison, the spectra of the mononegative ions of perylene (Fig. 1*A*), tetracene (Fig. 2*A*), anthracene (Fig. 3*A*), 3,4-benzopyrene (Fig. 4*A*), and pyrene (Fig. 5*A*) have been included. The spectrum of the 3,4-benzopyrene mononegative ion is new; the others have been reported.[7]

Solutions in sulphuric acid. Pyrene is readily soluble in sulphuric acid but decomposes within a few minutes, the colour of the solution changing from green to yellow. The green solution clearly displays the strong absorption of the proton complex at 22 kK. The solution of anthracene is slightly more stable than that of pyrene; its absorption spectrum can be measured with reasonable accuracy (Fig. 3*C*).

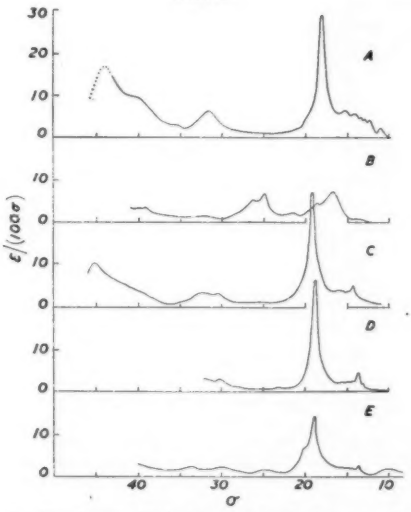
Perylene, tetracene, and 3,4-benzopyrene give stable solutions. On dilution with water and extraction with benzene the original hydrocarbons are recovered. When perylene dissolves in

[4] Kon and Blois, jun., *J. Chem. Phys.*, 1958, **28**, 743.
[5] Gold and Tye, *J.*, 1952, 2173, 2181.
[6] Dallinga, Mackor, and Verrijn Stuart, *Mol. Phys.*, 1958, **1**, 123; Verrijn Stuart and Mackor, *J. Chem. Phys.*, 1957, **27**, 826.
[7] Balk, Hoijtink, and Schreurs, *Rec. Trav. chim.*, 1957, **76**, 813.
[8] Mackor, Hofstra, and van der Waals, *Trans. Faraday Soc.*, 1958, **54**, 66.

sulphuric acid a green colour is observed which after a few seconds changes to violet. The spectrum does not alter when the violet solution is kept for several days (Fig. 1*C*).

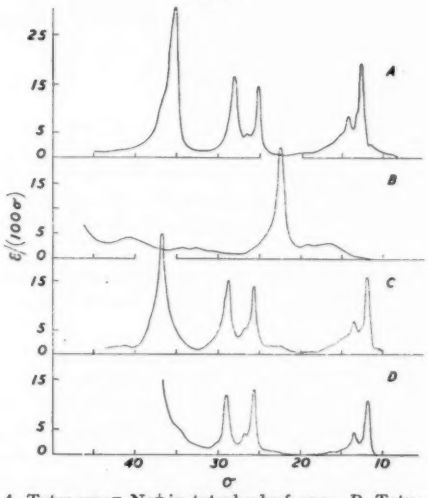
The spectrum of tetracene in sulphuric acid is a superposition of the spectra of two species. When the solution is kept for a few hours, a strong absorption band at 23 kK disappears and the bands of the positive ion become stronger; exposure to ultraviolet radiation for one minute has the same effect. The spectrum of the positive ion in sulphuric acid afterwards remains unaltered for several days (Fig. 2*C*) if the solution is kept in darkness. It is very likely that the strong absorption band at 23 kK is due to the initial formation of the proton complex.[6]

FIG. 1.



A, Perylene$^-$ Na^+ in tetrahydrofuran; *B*, Perylene in HF; *C*, Perylene in H_2SO_4; *D*, Perylene in $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air; *E*, Perylene in HF in contact with air.

FIG. 2.



A, Tetracene$^-$ Na^+ in tetrahydrofuran; *B*, Tetracene in HF; *C*, Tetracene in H_2SO_4; *D*, Tetracene in $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air.

In all diagrams the function ε/σ is plotted against σ, where ε is the molar absorption coefficient and σ is the wave number (in kK).

3,4-Benzopyrene in sulphuric acid displays a spectrum which very closely resembles that of the proton complex in hydrogen fluoride.[6] The spectra are represented in Fig. 4*C* and 4*B* respectively.

Naphthalene, phenanthrene, and chrysene were insoluble in concentrated sulphuric acid (see ref. 4). 1,2-Benzanthracene and 1,2:5,6-dibenzanthracene are only sparingly soluble and the solutions decompose rapidly. These hydrocarbons were not further investigated.

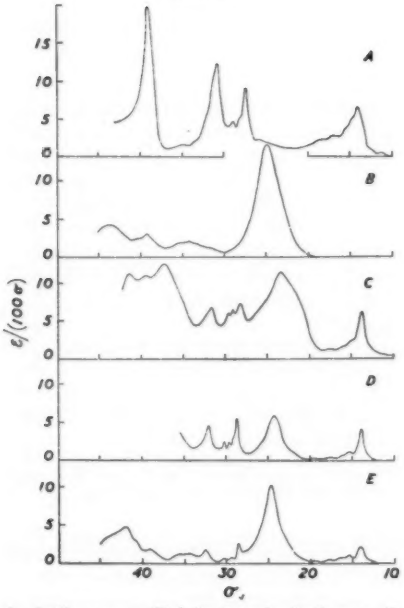
Solutions in anhydrous hydrogen fluoride. The spectra displayed in HF in the absence of oxygen by the proton complexes of perylene, tetracene, anthracene, 3,4-benzopyrene, and pyrene are in Figs. 1*B*—5*B*. The assignment of the spectral bands has been given.[6] In presence of oxygen the absorption bands of the proton complexes of perylene, tetracene, and anthracene rapidly become less intense while the absorption bands of their monopositive ions become more intense; no change was observed for 3,4-benzopyrene and pyrene when oxygen was introduced at 1 atm. The spectra of the solutions in oxygen-containing HF of perylene and anthracene are in Figs. 1*E* and 3*E*, respectively.

A few hours after introduction of oxygen at low pressures, and more rapidly at higher oxygen pressures, the spectra of the solutions, except perhaps for perylene, begin to change markedly. Dark precipitates are formed. Nevertheless, the formation of the monopositive ions appears to be reversible. For solutions of anthracene which have been in contact with oxygen for

1 hr., the original spectrum of the proton complex reappears when oxygen is eliminated by cooling and evacuating. In another experiment, at least 85% of the anthracene could be recovered from a solution in HF after it had been kept for 1 hr. in contact with oxygen at 45 atm. at 20° c.

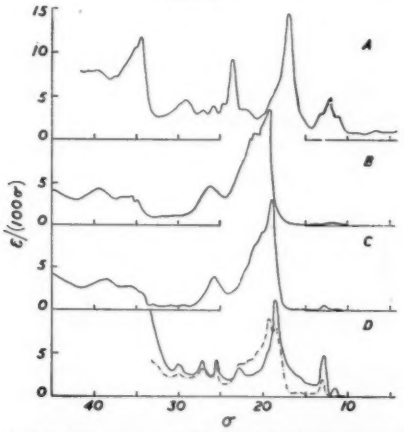
Solutions in trifluoroacetic acid with 22 moles % of BF_3,H_2O. If more than about 5 moles % of an equimolar mixture of BF_3 and H_2O are added to trifluoroacetic acid, the more highly basic

FIG. 3.



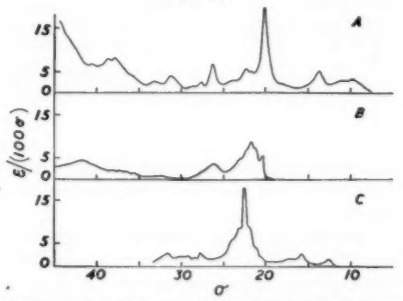
A, Anthracene$^-$ Na^+ in tetrahydrofuran; *B*, Anthracene in HF; *C*, Anthracene in H_2SO_4; *D*, Anthracene in $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air; *E*, Anthracene in HF, in contact with oxygen at 3 atm.

FIG. 4.



A, 3,4-Benzopyrene$^-$ Na^+ in tetrahydrofuran; *B*, 3,4-Benzopyrene in HF; *C*, 3,4-Benzopyrene in H_2SO_4; *D*, 3,4-Benzopyrene in $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air: —·— after 30 min.; —— after 24 hr

FIG. 5.



A, Pyrene$^-$ Na^+ in tetrahydrofuran; *B*, Pyrene in HF; *C*, Pyrene in $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air.

hydrocarbons will dissolve in the mixture as their proton complexes. In absence of oxygen the solutions display spectra resembling those in anhydrous HF. A mixture with 22 moles % of BF_3,H_2O was used. The Hammett acidity function of this mixture, determined spectroscopically by use of picramide ($pK_a = -9{\cdot}22$) as indicator, is $H_0 = -9{\cdot}9$. When oxygen is introduced into these solutions of perylene, tetracene, anthracene, 3,4-benzopyrene, and pyrene the spectra are drastically changed. In all cases these spectra, which are in Figs. 1*D*—4*D* and 5*C*, respectively, are very similar to those of the corresponding mononegative ions.

The solutions of perylene, tetracene, and 3,4-benzopyrene are stable. For the last two the reaction with oxygen is rather slow; after 1 hr. the reaction is only 50% complete. For anthracene and pyrene, too, the reaction was incomplete after 1 hr., but solutions of these hydrocarbons were not stable; after 24 hr. they had decomposed.

The broken line of Fig. 4*D* shows that the proton complex of 3,4-benzopyrene after 30 minutes' contact with oxygen is only partly (*ca.* 50%) converted into the monopositive ion. After 24 hr. the bands of the proton complex have disappeared; the new spectrum (full line) is very similar to that of the mononegative ion of Fig. 4*A* (the first absorption band of the proton complex is at 19·20 kK, while the strong absorption band of the positive ion is at 18·35 kK). In comparison with the absorption bands of the mononegative ion the bands of the monopositive ion are shifted a few kK towards the blue region.

Similar observations can be made for pyrene. The spectrum of Fig. 5*C* is a superposition of the spectrum of proton complex (*ca.* 10%) and that of its monopositive ion.

Discussion

One may expect theoretically that the electronic spectra of the monopositive and mononegative ions of alternant hydrocarbons are practically identical.[9] One must therefore conclude that on dissolving perylene, tetracene, anthracene, 3,4-benzopyrene, and pyrene in $CF_3{\cdot}CO_2H$–BF_3,H_2O, containing oxygen, their monopositive ions are formed, because the electronic spectra of these solutions are very similar to those of the corresponding mononegative ions. Apparently, electron transfer may occur when strongly basic hydrocarbons are dissolved in strongly acidic oxidizing solvents. The oxygen molecule in strongly acidic solvents acts as an electron acceptor, probably giving rise to the protonated forms of O_2^- or O_2^{2-}.

Similar phenomena are observed when these hydrocarbons are dissolved in concentrated sulphuric acid, where SO_3 may act as an electron acceptor[10] and in hydrogen fluoride containing oxygen.[6] The oxidizing properties of the latter solvents, however, must be less strong than those of oxygen in $CF_3{\cdot}CO_2H$–BF_3,H_2O mixtures. This may be demonstrated from the results for perylene and 3,4-benzopyrene. In this mixture both hydrocarbons are almost quantitatively oxidized to their monopositive ions. In sulphuric acid and in HF with oxygen, on the other hand, only perylene forms a monopositive ion whereas 3,4-benzopyrene dissolves as its proton complex.

Our results indicate that in strong oxidising acids an equilibrium exists between the proton complex MH^+ and the monopositive ion M^+. Compared with the concentrations of MH^+ and M^+ the concentration of hydrocarbon molecules M is negligible. If one assumes that the acceptor adds one electron the equilibrium can formally be written as:

$$M^+ + A^- + H^+ \rightleftharpoons MH^+ + A \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The constant for this equilibrium follows from the equation:

$$\ln K = \ln K_b + \varepsilon_{ox} \times \frac{F}{RT} + \text{constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

or in decadic logarithms:

$$\log K = \log K_b + 16{\cdot}95\ \varepsilon_{ox} + \text{constant} \quad . \quad . \quad . \quad . \quad . \quad (3)$$

in which K_b and ε_{ox} stand for the basicity constant and the standard oxidation potential of the hydrocarbon, respectively. The constant in eqn. (3) depends on the natures and the concentrations of proton donor and electron acceptor.

The relative values of the equilibrium constant K can be calculated for a great number of aromatic hydrocarbons by using known basicity constants[8] and Lund's oxidation

[9] Weijland, Thesis, Free University, Amsterdam, 1958; Hoijtink, Colloque International sur le Calcul des Fonctions d'Ondes Moléculaires; Ed. C.N.R.S., Paris, 1958, 237.

[10] Aalbersberg, Hoijtink, Mackor, and Weijland, following paper.

XUM

potentials.[11] The values of K for the hydrocarbons studied by us, which combine a high value of K_b and a low value of ϵ_{ox}, are in the Table. If the formal eqn. (1) corresponds to reality, the values of K are a relative measure of the concentration ratio between proton complex and monopositive ion.

Basicity constants, oxidation potentials, and relative values of log K, *of reaction* (1).

Compound	log K_b [a]	E_{ox} [b]	log K + const.
3,4-Benzopyrene	6·5	0·76	19·4
Anthracene	3·8	0·84	18·0
Pyrene	2·1	0·86	16·7
Perylene	4·4	0·63 [c]	15·1
Tetracene	5·8	0·54	15·0

[a] Taken from ref. 8. [b] In volts against the silver–0·1N-Ag^+ electrode in acetonitrile; solvent: acetonitrile; taken from ref. 11. [c] The oxidation potential of perylene has been calculated from its reduction potential, by use of the linear relation between reduction and oxidation potentials of alternant hydrocarbons (Hoijtink, *Rec. Trav. chim.*, 1958, **77**, 555).

From the Table one must expect that (under equal conditions) the ratio of the concentrations $(MH^+)/(M^+)$ will be largest for 3,4-benzopyrene and smallest for perylene or tetracene. This is confirmed by the experiments, which show that the latter compounds (in particular perylene) are readily oxidized to their monopositive ions, whereas 3,4-benzopyrene is not. Anthracene and pyrene, which according to the values in the Table must have intermediate values of $(MH^+)/(M^+)$, are indeed less easily oxidized than perylene. Anthracene is only partially oxidized in HF by O_2 under conditions that cause complete oxidation of perylene. Similar observations were made in concentrated sulphuric acid, showing that anthracene is intermediate between perylene and 3,4-benzopyrene in its properties as an electron donor.

It is difficult to draw more quantitative conclusions. On the one hand solutions of anthracene and pyrene in strong oxidizing acids are not stable and on the other the formation of the monopositive ions is in several cases slow and may be photocatalysed. One does not know therefore whether equilibrium has been established. The present investigations make it clear that the paramagnetism found for anthracene, pyrene, and 3,4-benzopyrene in concentrated sulphuric acid by Kon and Blois [4] is due to a small fraction of the hydrocarbon dissolved; especially for 3,4-benzopyrene only a very small fraction can be present as the monopositive ion.

One of us (W. P. W.) thanks N.V. Philips Gloeilampenfabrieken, Eindhoven, for financial support. This work was supported by "Netherlands Organisation for the Advancement of Pure Research" (Z. W. O.).

CHEMICAL LABORATORY, FREE UNIVERSITY, AMSTERDAM.
KONINKLIJKE/SHELL-LABORATORIUM, AMSTERDAM.

[*Received, February 9th*, 1959.]

[11] Lund, *Acta Chem. Scand.*, 1957, **11**, 1323.

612. *Complexes of Aromatic Hydrocarbons with Strong Lewis Acids.*

By W. Ij Aalbersberg, G. J. Hoijtink, E. L. Mackor, and W. P. Weijland.

The electronic absorption spectra of complexes of 1,2-benzanthracene, anthracene, perylene, tetracene, and 3,4-benzopyrene with strong Lewis acids such as BF_3, PF_5, $SbCl_5$, and SO_3 have been investigated. Two sorts of complex are formed: a covalent complex with the Lewis acid, and a complex in which the hydrocarbon is present as its monopositive ion.

The spectra of the covalent complexes very closely resemble those of the corresponding proton complexes. This implies that, for the hydrocarbons investigated, proton addition and the addition of a Lewis acid take place at the same carbon atom of the hydrocarbon molecule. The competition between the formation of covalent complexes and monopositive ions is discussed on the basis of the basicity constants and oxidation potentials of the aromatic hydrocarbons.

Tetracene in dimethyl sulphate with sulphur trioxide displays a spectrum which is a superposition of the spectra of the mono- and the di-positive ion.

Various aromatic hydrocarbons form intensely coloured complexes with Lewis acids such as ferric chloride, stannic chloride, and antimony pentachloride.[1] Their structures remained obscure until Weissman, de Boer, and Conradi [2] reported that the solid complex of perylene with antimony pentachloride is paramagnetic. In addition, the solution of the complex in nitrobenzene displays practically the same absorption spectrum as the perylene monopositive ion formed on dissolving the hydrocarbon in concentrated sulphuric acid.[3] We therefore conclude that on addition of a strong Lewis acid, such as antimony pentachloride, to a solution of perylene in nitrobenzene, electron transfer takes place from the hydrocarbon molecule to the Lewis acid and the monopositive ion is formed.

The reaction of a number of highly basic aromatic hydrocarbons with compounds such as BF_3, PF_5, $SbCl_5$, and SO_3 will now be discussed. The experimental results may illuminate the nature of these complexes of aromatic hydrocarbons with strong Lewis acids.

Experimental

Hydrocarbons were from the previous source.[4]

Complexes with Boron Trifluoride and Phosphorus Pentafluoride in 1,2-Dichloroethane.—Most of the solutions were prepared in a Pyrex apparatus to which a quartz cell (optical path 1 cm.) was connected by a graded Pyrex-to-quartz seal. The Pyrex apparatus had no glass joints or stopcocks and was provided with four magnetic break-seals. The whole equipment was baked out at 450° under high vacuum ($\sim 10^{-6}$ mm. Hg) for two days.

Through one break-seal about 100 ml. of 1,2-dichloroethane (prefractionated and carefully dried on P_2O_5 *in vacuo*) was distilled into the equipment. Another break-seal was used to introduce a weighed amount of hydrocarbon. The concentration of the hydrocarbon was about 10^{-4}M. The apparatus was then sealed off and the spectrum of the solution was measured. Next, boron trifluoride (Fluka A.G.; carefully fractionated) or phosphorus pentafluoride was introduced through the third break-seal, while the apparatus was kept in the dark. The pressure was read from a constant-volume manometer. The concentration of BF_3 in 1,2-dichloroethane at 20·0°/1 atm. is $3{\cdot}7 \times 10^{-2}$M.

After the equipment had been sealed off the spectrum of the solution was recorded. Finally the fourth break-seal could be used for the removal of the gas by freezing the solution in solid carbon dioxide–alcohol and evacuating (3 times).

Phosphorus pentafluoride was prepared by decomposing Phosfluorogen (Ozark-Mahoning Co.),

[1] (*a*) Hilpert and Wolf, *Ber.*, 1913, **46**, 2215; (*b*) Radulescu, *Ber.*, 1931, **64**, 2223.
[2] Weissman, de Boer, and Conradi, *J. Chem. Phys.*, 1957, **26**, 963.
[3] Hoijtink and Weijland, *Rec. Trav. chim.*, 1957, **76**, 836.
[4] Aalbersberg, Hoijtink, Mackor, and Weijland, preceding paper.

XUM

a substituted benzidinediazonium salt of phosphorus hexafluoride, at about 100°. It was purified by freezing (−180°), evacuating, and distilling (3 times).

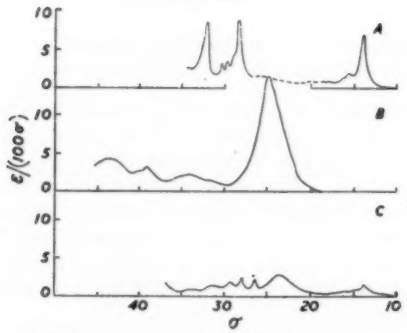
The spectra were recorded on a Cary spectrophotometer (Model 11 or 14).

Complexes with Antimony Pentachloride and Sulphur Trioxide.—No special precautions were taken in the preparation of solutions of tetracene and perylene in nitrobenzene with $SbCl_5$ or in dimethyl sulphate with SO_3. In nitrobenzene the complexes with $SbCl_5$ slowly decompose and the extinctions were calculated by extrapolation to zero time. The extrapolated values obey the Beer–Lambert law in the concentration range $0{\cdot}01$—$0{\cdot}5 \times 10^{-4}$M.

The spectra were measured on a Unicam SP.500 spectrophotometer.

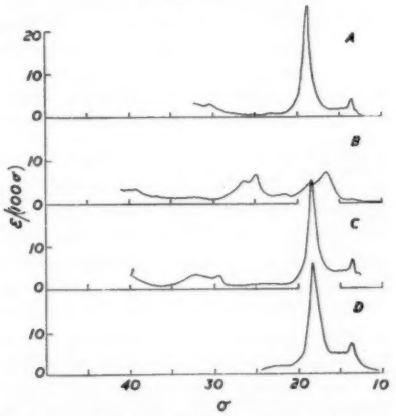
Results.—The spectra of the complexes of anthracene, perylene, tetracene, and 3,4-benzopyrene with BF_3 (1 atm.) in 1,2-dichloroethane, and with $SbCl_5$ in nitrobenzene, are shown in Figs. 1, 2, 3, and 4, respectively. The spectrum of a solution of tetracene in dimethyl sulphate

FIG. 1.



A, Monopositive ion of anthracene (solvent $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air, by extrapolation); *B*, Proton complex of anthracene (solvent HF); *C*, Anthracene + BF_3 in 1,2-dichloroethane in the dark.

FIG. 2.



A, Monopositive ion of perylene (solvent $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air); *B*, Proton complex of perylene (solvent HF); *C*, Perylene + BF_3 in 1,2-dichloroethane after irradiation; *D*, Perylene + $SbCl_5$ in nitrobenzene.

In all diagrams the function ε/σ is plotted against σ, where ε is the molar absorption coefficient and σ is the wave number (in kK).

with SO_3 is given in Fig. 5*C*. The spectrum of perylene in dimethyl sulphate in the presence of SO_3 is identical with that of Fig. 2*D*. For comparison the spectra of the monopositive ions [4] and the proton complexes [5] of anthracene,* perylene, tetracene, and 3,4-benzopyrene are also represented in Figs. 1—4. The spectrum of the tetracene dinegative ion [6] is given in Fig. 5*B*.

Complexes with BF_3 *and* PF_5. The reaction of BF_3 and PF_5 with the hydrocarbons in 1,2-dichloroethane appears to be perfectly reversible. If the gas is removed from the solution by freezing and evacuation or if an excess of water is added, the original spectrum of the hydrocarbon reappears. No decomposition was observed after short exposure to ultraviolet radiation (medium-pressure mercury arc).

Water must be rigorously excluded since BF_3 and PF_5 with water form strong proton acids, *e.g.*, BF_3,H_2O. These acids might react with the strongly basic hydrocarbons to give their proton complexes.[5]

* Anthracene in $CF_3{\cdot}CO_2H$–BF_3,H_2O (22 moles %) containing oxygen [4] is present as an equimolar mixture of proton complex and monopositive ion. This spectrum of the anthracene monopositive ion of Fig. 1*A* has been obtained by extrapolation to 100% conversion.

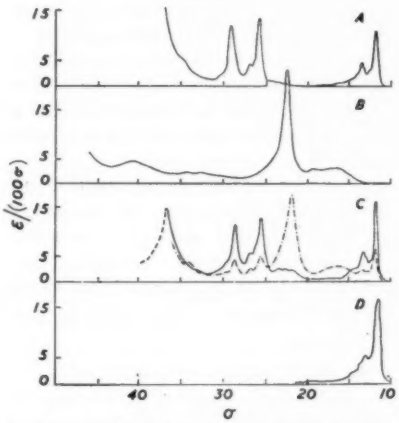
[5] Dallinga, Mackor, and Verrijn Stuart, *Mol. Phys.*, 1958, **1**, 123; Verrijn Stuart and Mackor, *J. Chem. Phys.*, 1957, **27**, 826.

[6] Balk, de Bruijn, and Hoijtink, *Mol. Phys.*, 1958, **1**, 151.

In view of the extreme care taken to exclude water it is highly improbable that proton complexes should be formed.* Nevertheless in nearly all cases the solutions, at least initially, display spectra remarkably similar to those of the proton complexes. In particular the more basic hydrocarbons show this behaviour, as Fig. 4*C* shows for 3,4-benzopyrene. Since water is absent, these spectra are probably due to the formation of covalent BF_3–hydrocarbon complexes.

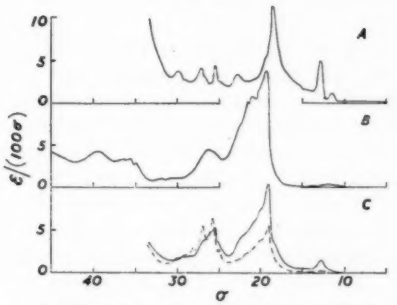
The covalent complex of 3,4-benzopyrene appears to be very stable; exposure to ultraviolet

FIG. 3.



A, Monopositive ion of tetracene (solvent $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air); *B*, Proton complex of tetracene (solvent HF); *C*, Tetracene + BF_3 in 1,2-dichloroethane, — · — · — before irradiation, —— after irradiation; *D*, Tetracene + $SbCl_5$ in nitrobenzene.

FIG. 4.



A, Monopositive ion of 3,4-benzopyrene (solvent $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air); *B*, Proton complex of 3,4-benzopyrene (solvent HF); *C*, 3,4-benzopyrene in 1,2-dichloroethane; — · — · — with BF_3 in the dark, —— with PF_5 after irradiation.

radiation hardly affects the spectrum. The solutions of the other hydrocarbons mentioned in Table 1, on the other hand, are not stable and the spectra of the solutions change slowly. This reaction is photo-catalysed; on exposure of the solutions to ultraviolet radiation the spectra

TABLE 1. *Percentages of hydrocarbon present as molecule, covalent complex, and monopositive ion for different hydrocarbons in* 1,2-*dichloroethane at* 1 *atm. of* BF_3.

	Before irradiation			After irradiation		
Hydrocarbon	M	M,BF_3	M^+	M	M,BF_3	M^+
1,2-Benzanthracene	⩾98	⩽2 ‡	⩽1 ‡	92 *	⩽3 ‡	⩽1 ‡
Anthracene	55	25	20	35 *	35 *	30 *
Perylene	100	⩽1	⩽1	⩽1	⩽1	⩾98
Tetracene	⩽5	70	25	⩽2 †	⩽5 †	⩾93
3,4-Benzopyrene	58	40	⩽2	56	40	~5

* On irradiation the solute is partly precipitated.

† Could not be analysed accurately.

‡ The spectrum (not recorded in the Figures) shows very weak absorption bands at 18·80 and 21·75 kK similar to the bands of the proton complex. The spectrum of either monopositive or mononegative ion is not known. By comparison with the spectra of the monopositive ion of anthracene [4] and of the mononegative ion of dibenzanthracene, measured by Paul, Lipkin and Weissman,[19] it seems certain that the mononegative as well as the monopositive ions of 1,2-benzanthracene should have a fairly strong absorption band at frequencies lower than 15 kK. Below 16 kK no absorption was observed and we conclude that less than 1% of the molecule is converted into its monopositive ion.

display absorption bands of the monopositive ions.[4] For tetracene this is illustrated in Fig. 3*C*. After irradiation the spectrum is practically identical with that of the monopositive ion.[4]†

* No water could be detected in the solution by the Karl Fischer titration. This means that the concentration of BF_3 in our experiment is at least 40 times that of water.

† In nitromethane the formation of the positive ion proceeds much faster. In this case, however, the spectra alter with time, owing to side reactions with the solvent.

XUM

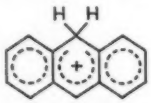
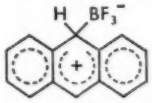
It is clear that the spectra displayed by the solutions of these hydrocarbons in 1,2-dichloroethane in the presence of BF_3 are superpositions of the spectra of the uncomplexed molecules, the covalent complexes, and the monopositive ions. Table 1 gives the compositions of the solutions in the presence of BF_3 before and after irradiation. In general, bands to be assigned to covalent complexes and monopositive ions are easily recognized. The bands of the uncomplexed molecules are weaker than those of the corresponding complexes and partly coincide with the latter. Fractions of uncomplexed molecules below 10% cannot be analysed accurately.

The preliminary results obtained with PF_5 are similar to those with BF_3.

Discussion

From the spectra in Figs. 1, 2, 3, and 4 and the data in Table 1 it appears that two different species are formed by the reaction of aromatic hydrocarbons with strong Lewis acids, *viz.*, covalent complexes and monopositive ions.

Covalent Complexes.—The spectra of the complexes of the hydrocarbons with BF_3 (or PF_5) in 1,2-dichloroethane before irradiation closely resemble the spectra of the proton complexes.[5] Recent investigations [5,7,8] have firmly established Gold and Tye's [9] idea that in proton complexes the proton is linked to one of the carbon atoms by a covalent bond. From proton spin resonance [8] it appeared that the methylenic group (formed by proton addition to one of the carbon atoms) has an aliphatic character. The positions and

(I)   (II)

intensities of the absorption bands in the visible and near ultraviolet regions have been shown to be representative of the conjugated part of the proton complex.[5] Since the spectra of the proton complexes and the corresponding covalent BF_3 complexes are closely similar (cf. Figs. 1—4), we conclude that the BF_3 molecule is added to the same carbon atom of the aromatic hydrocarbon as the proton. Thus the structures of the covalent complexes of anthracene, tetracene, and 3,4-benzopyrene (perylene in the presence of BF_3 does not form a covalent complex) must be comparable with the structures of the corresponding proton complexes.[5] For instance the proton complex and the covalent complex with BF_3 of anthracene should have the structures (I) and (II).

TABLE 2. *Basicity constants, oxidation potentials, relative values of* log *K of reaction* (4) *and other experimental values in* 1,2-*dichloroethane at* 1 *atm.* BF_3.

Hydrocarbon	log K_b [a]	log $\frac{[MBF_3]}{[M]}$	ε_{ox} [b]	log $\frac{[M^+]}{[M]}$ [d]	const. + log K	log $\frac{[MBF_3]}{[M^+]}$ [d]
1,2-Benzanthracene ...	2·3	$<-1{\cdot}7$	0·92	$<-1{\cdot}7$	17·9	—
Anthracene	3·8	$\sim-0{\cdot}3$	0·84	$\sim$0·0	18·0	$\sim$0·0
Perylene	4·4	$<-1{\cdot}7$	0·63 [c]	$\geqslant 1{\cdot}7$	15·1	$<-1{\cdot}7$
Tetracene	5·8	$\sim+1{\cdot}4$	0·54	$\geqslant 1{\cdot}7$	15·0	$\sim-1{\cdot}0$
3,4-Benzopyrene	6·5	$\sim-0{\cdot}2$	0·76	$\sim-1{\cdot}0$	19·4	$\sim+0{\cdot}9$

[a] From ref. 7. [b] In volts against the Ag–0·1N-Ag^+ electrode in acetonitrile; solvent: acetonitrile. Taken from ref. 10*a*. [c] The oxidation potential of perylene has been calculated from its reduction potential by using the linear relation between reduction and oxidation potentials of alternant hydrocarbons (cf. ref. 10*b*). [d] Values obtained after irradiation.

The stability of the covalent complex is governed by the constant K_c of the equilibrium between uncomplexed molecule M plus Lewis acid A and the covalent complex MA:

$$M + A \rightleftharpoons MA \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (I)$$

[7] Mackor, Hofstra, and van der Waals, *Trans. Faraday Soc.*, 1958, **54**, 66.
[8] MacLean, van der Waals, and Mackor, *Mol. Phys.*, 1958, **1**, 247.
[9] Gold and Tye, *J.*, 1952, 2173, 2181.
[10] (*a*) Lund, *Acta Chem. Scand.*, 1957, **11**, 1323; (*b*) Hoijtink, *Rec. Trav. chim.*, 1958, **77**, 555.

One would expect the basicity constant K_b (Table 2, column 1) to be a qualitative measure of the constant K_c for these hydrocarbons. In Table 2 values of log K_b and log {[MBF_3]/[M]} (taken from Table 1) are compared. The hydrocarbons are arranged in sequence of increasing basicity. 1,2-Benzanthracene (a hydrocarbon with a relatively low basicity) does not form complexes with BF_3, whereas tetracene and 3,4-benzopyrene, both having much higher basicity constants, do form covalent complexes. Deviations from the basicity sequence as occurring in Table 2 are probably due to the fact that steric factors are more important in BF_3 addition than in proton addition.

Monopositive Ions.—In nitromethane and in nitrobenzene (solvents with a relatively high dielectric constant) or in 1,2-dichloroethane on irradiation the aromatic hydrocarbons may be partly or completely converted into their monopositive ions. The spectra of the hydrocarbons anthracene, tetracene, and perylene in the presence of strong Lewis acid such as BF_3, PF_5, and $SbCl_5$ closely resemble those of the monopositive ions reported previously.[4] Here the Lewis acid may act as electron acceptor. The experiments have shown that these reactions are perfectly reversible. If the Lewis acid is assumed to take up one electron from the hydrocarbon the following equilibrium exists: *

$$M + A \rightleftharpoons M^+ + A^- \quad . . . . . (2)$$

For a given Lewis acid the oxidation potentials of the hydrocarbons [10] (Table 2) will give a qualitative measure of the stability of the monopositive ions. If we assume that after irradiation of the solution of the hydrocarbon in 1,2-dichloroethane in the presence of BF_3 the equilibrium of reaction (2) is reached, the value of log {[M^+]/[M]} (Table 2) should run parallel with the corresponding value of ε_{ox}. From Table 2 it appears that 3,4-benzopyrene and 1,2-benzanthracene are much less easily oxidized than either perylene or tetracene. Anthracene seems to be a better electron donor than would be expected on the basis of its oxidation potential.

The experiments have not provided conclusive evidence about the exact nature of the negative counter-ions formed in reaction (2).

The low rate of this reaction in 1,2-dichloroethane may be due to the fact that the negative counter-ion A^- must be stabilized, *e.g.*, by a combination with a second negative ion:

$$2BF_3^- \rightleftharpoons B_2F_6^{2-} \quad . . . . . (3)$$

In solvents with a high dielectric constant such as nitromethane or nitrobenzene the ion is probably stabilized by solvation.

Equilibrium between Monopositive Ions and Covalent Complexes.—The formation of monopositive ions will be favoured by a low oxidation potential and a relatively low basicity. Since, generally, a low oxidation potential corresponds with a relatively high basicity only few hydrocarbons will be converted quantitatively into their monopositive ions on the addition of Lewis acids. The same conclusion was drawn [4] for formation of monopositive ions in strong proton donors. In the latter case a competition occurs between proton addition and the formation of monopositive ions.

The constant for the equilibrium

$$M^+ + A^- \rightleftharpoons MA \quad . . . . . (4)$$

will give a qualitative measure of the ratio [MA]/[M^+]. Steric factors being neglected, this constant follows from the equation: [4]

$$\log K = \log K_b + 16{\cdot}95\varepsilon_{ox} + \text{constant} \quad . . . . . (5)$$

in which K_b and ε_{ox} stand for the basicity constant and the oxidation potential of the hydrocarbon, respectively. The constant term depends on the choice of the Lewis acid, its concentration, the nature of the solvent, etc.

* In 1,2-dichloroethane especially, the ions M^+ and A^- will be strongly associated.

XUM

In Table 2, column 5, the relative values of log K are listed. These values again show a trend similar to that of the rather rough estimates of the ratios $[MBF_3]/[M^+]$ listed in the last column.

Bivalent Positive Ions.—So far only the formation of monopositive ions was discussed. When, however, SO_3 is added to a solution of tetracene in dimethyl sulphate, a mixture of mono- and di-positive ions is formed. In Fig. 5 the spectrum of this solution is compared with the spectra of the tetracene monopositive and dinegative ion.[6] Since according to the theory the spectra of the dipositive and dinegative ions (as well as the spectra of the monopositive and mononegative ions) of alternant hydrocarbons will be practically identical [11] it may be concluded from Fig. 5 that the reaction of tetracene in dimethyl sulphate leads to a mixture of the mono- and the di-positive ion. Under the same conditions perylene gives only the monopositive ion. Apparently the oxidation potential of the perylene monopositive ion is higher than that of the tetracene monopositive ion.

These investigations [4] on the formation of hydrocarbon positive ions as well as previous investigations on the formation of hydrocarbon negative ions [6,12,13,14] suggest that electron

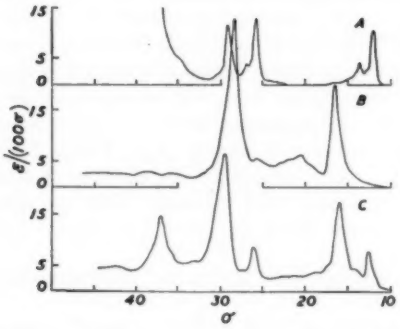


FIG. 5.

A, Monopositive ion of tetracene (solvent $CF_3{\cdot}CO_2H$–BF_3,H_2O in contact with air); *B*, Tetracene^{2-} 2(Na^+) in tetrahydrofuran; *C*, Tetracene + SO_3 in dimethyl sulphate.

transfer will be a major step in many organic reactions. This is also demonstrated by investigations by Buck, Lupinski, and Oosterhoff,[15] who found that the highly coloured complexes of substituted diphenyl- and of tetraphenyl-ethylene with acids, halogens, and nitro-compounds are in many cases paramagnetic.

The conclusions drawn in this paper also confirm Wizinger's suggestion [16] that electron transfer takes place in the reaction of aromatic compounds with Lewis acids and Weiss's [17] suggestion that electron transfer is the first step in organic oxidative reactions.

CHEMICAL LABORATORY, FREE UNIVERSITY, AMSTERDAM.
KONINKLIJKE/SHELL-LABORATORIUM, AMSTERDAM.
[*Received, February 9th*, 1959.]

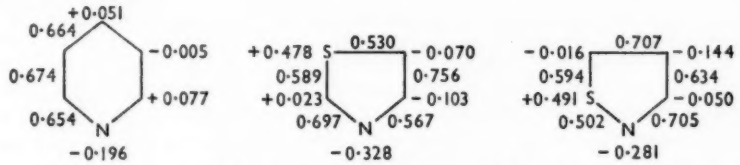
[11] Weijland, Thesis, Free University, Amsterdam, 1958.
[12] Paul, Lipkin, and Weissman, *J. Amer. Chem. Soc.*, 1956, **78**, 116.
[13] de Boer and Weissman, *J. Amer. Chem. Soc.*, 1958, **80**, 4549, and related papers.
[14] Balk, de Bruijn, and Hoijtink, *Rec. Trav. chim.*, 1957, **76**, 907; Hoijtink, de Boer, van de Meij, and Weijland, *ibid.*, 1956, **75**, 487, and related papers.
[15] Buck, Lupinski, and Oosterhoff, *Mol. Phys.*, 1958, **1**, 197.
[16] Wizinger, *Organische Farbstoffe*, 1933, 48—51.
[17] Weiss, *J.*, 1942, 245; *Proc. Roy. Soc.*, 1954, *A*, **222**, 128.

613. *Isothiazole: A New Mononuclear Heterocyclic System.*

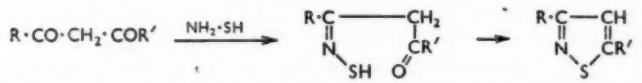
By A. Adams and R. Slack.

Many derivatives of isothiazole (1,2-thiazole), a hitherto unknown heterocyclic system, have been prepared, and the parent base and its 3-methyl derivative have been characterized.

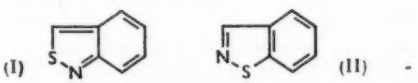
Mononuclear isothiazoles (1,2-thiazoles) have not hitherto been described, but a theoretical consideration of the properties of the parent led us to believe that it should be a reasonably stable molecule. Thus, the electronic similarity between –S– and –CH=CH– particularly in aromatic systems, has frequently been discussed (*e.g.*, by Longuet-Higgins [1]), and isothiazole might, therefore, be expected to resemble pyridine in many of its properties. A simplified calculation * of electron densities and mobile bond orders of the unsubstituted molecule emphasized its inherent stability, and its similarity to both pyridine and thiazole (cf. annexed diagram).



The unknown thiohydroxylamine would perhaps provide the most direct route to the system, but even this is doubtful since our experience of similar cyclizations suggests that



hydrogen sulphide is almost always lost in preference to water. The use of a thioketone would eliminate this difficulty but would introduce added complications. We therefore adopted two different methods of approach and have succeeded in preparing both isothiazole itself and a series of its derivatives.



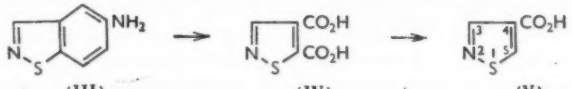
The first route [2] depended on disruptive oxidation of a substituted benzisothiazole. There are two series of benzisothiazoles, derived from benz[*c*]isothiazole (I) and benz[*d*]-isothiazole (II). The *o*-quinonoid system of the former made it likely that this compound would be completely ruptured by oxidation; and the latter, weakened in the *Bz*-ring by an anionoid substituent, appeared to be more suitable. 5-Aminobenz[*d*]isothiazole (III) was prepared by the known, but tedious route (*o*-chlorobenzaldehyde ⟶ 2-chloro-

* In these simplified calculations, overlap has been neglected. The following parameters were used for the Coulomb integrals. $\alpha_O = \alpha$; $\alpha_N = \alpha + 0{\cdot}5\beta$; $\alpha_S = \alpha + 1{\cdot}1\beta$. These were suggested by Professor C. A. Coulson (personal communication), the latter value being derived from that of α_O used by Orgel *et al.* (*Trans. Faraday Soc.*, 1951, **47**, 113) by a comparison of the electronegativities of oxygen and sulphur. A somewhat lower value for α_S might be more acceptable but would only slightly reduce the calculated charges without altering the relation between them. It is realized that our parameters, and therefore the calculated charges and bond orders, vary slightly from those used by Pullman and Metzger (*Bull. Soc. chim. France*, 1948, **15**, 1021) for thiazole calculations, but we believe that they are more soundly derived. The only difference between the two sets of results lies in the relative interchange of charge on the thiazole $C_{(4)}$ and $C_{(5)}$ atoms. The large difference between these charges and that on $C_{(2)}$, and the magnitude of the bond orders, remain virtually unaltered.

[1] Longuet-Higgins, *Trans. Faraday Soc.*, 1949, **45**, 173.
[2] Cf. Adams and Slack, *Chem. and Ind.*, 1956, 1232.

XUM

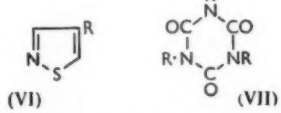
5-nitrobenzaldehyde ⟶ 2,2′-diformyl-4,4′-dinitrodiphenyl disulphide ⟶ 2-formyl-4-nitrosulphenyl bromide ⟶ 5-nitrobenz[*d*]isothiazole ⟶ 5-aminobenz[*d*]isothiazole) and its oxidation with alkaline potassium permanganate took place smoothly to give isothiazole-4,5-dicarboxylic acid (IV). Isolation of this acid was greatly simplified by the extreme insolubility of its monosodium salt which, surprisingly, recrystallized unchanged



(III) (IV) (V)

from 2N-sulphuric acid. Monodecarboxylation gave isothiazole-4-carboxylic acid (V) (cf. decarboxylation of 3-methylisothiazole-5-carboxylic acid, p. 3064), but many varied attempts at further decarboxylation were unsuccessful. The acid (V) was, therefore, degraded by the normal Curtius sequence to 4-aminoisothiazole. Hofmann's method from the amide (VIa) was unsuccessful. Methyl isothiazole-4-carboxylate (VIb) and isothiazole-4-carboxyhydrazide (VIc) and -4-carboxyazide (VId) were prepared by standard methods, and the corresponding benzylurethane (VIe) was smoothly hydrolysed to the amine (VIf) by hydrogen bromide in acetic acid.

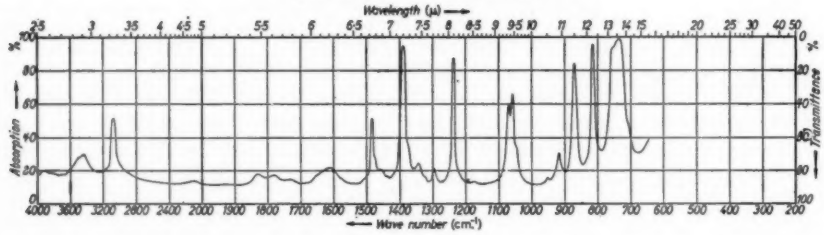
R	R
a, $CO{\cdot}NH_2$	f, NH_2
b, CO_2Me	g, $NH{\cdot}CO_2Et$
c, $CO{\cdot}NH{\cdot}NH_2$	h, $N(CO)_2C_6H_4$
d, CON_3	j, $NH{\cdot}SO_2{\cdot}C_6H_4{\cdot}NH_2$-*p*
e, $NH{\cdot}CO_2{\cdot}CH_2Ph$	k, H



(VI) (VII)

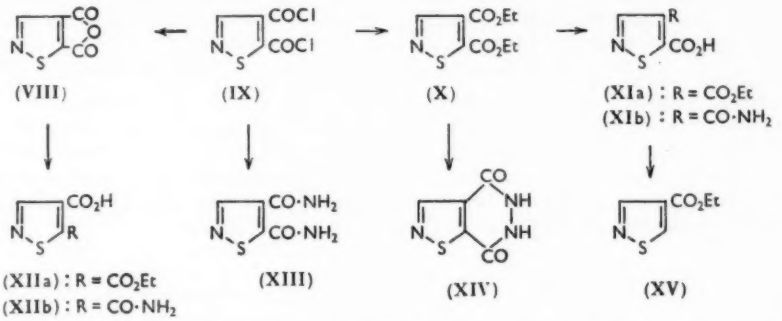
The ethylurethane (VIg) resisted hydrolysis, and 4-phthalimidoisothiazole (VIh) was obtained from the azide only in poor yield, the trimeric isocyanate (VII; R = isothiazolyl) being occasionally formed instead. The imide (VIh) could be hydrolysed to the amine, but again the overall yield from azide was low. 4-Aminoisothiazole was also converted into its acetyl and benzoyl derivatives and into the sulphonamide (VIj). Treatment of the diazotized amine with hypophosphorous acid gave isothiazole (VIk), a colourless, highly refractive, mobile liquid with an odour reminiscent of both pyridine and thiazole. Its infrared spectrum is shown in the Figure; ultraviolet data are given on p. 3067. It readily formed crystalline derivatives with mercuric chloride, chloroplatinic acid, and chloroauric acid.

Infrared spectrum of isothiazole.

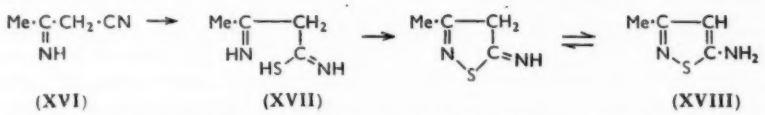


Attempts to remove selectively the 4-substituent of the diacid (IV) were unsuccessful. Thus, this acid was converted by standard methods into the dichloride (IX), the diethyl ester (X), and the diamide (XIII). Partial hydrolysis of the diester gave the 4-ethyl monoester (XIa) which on decarboxylation gave ethyl isothiazole-4-carboxylate (XV), converted by hydrazine hydrate into its hydrazide (VIc). The monoester was also converted into the amide-acid (XIb), which gave isothiazole-4-carboxyamide when heated. The monoester (XIa) was also prepared from the monosilver salt of the diacid (IV) and ethyl iodide. The diester (X) with hydrazine hydrate gave the cyclic hydrazide (XIV).

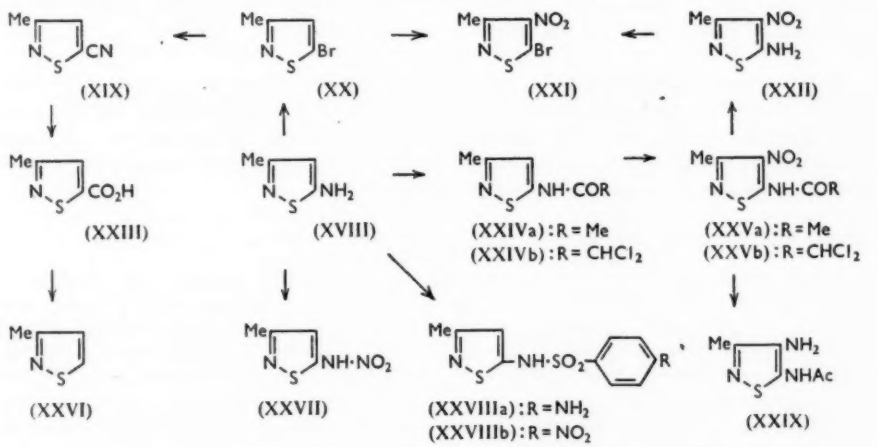
The anhydride (VIII) was prepared from the dichloride and yellow mercuric oxide and was converted into the 5-monoester (XIIa) and the related amide-acid (XIIb), but neither of these could be decarboxylated.



These failures to prepare 5-monosubstituted isothiazoles made us seek a more direct synthesis of this series. β-Iminothiobutyramide (XVII) was prepared from the known nitrile (XVI) and was converted by chloramine into 5-amino-3-methylisothiazole (XVIII). This conversion, at first believed to take place by successive elimination of ammonia and hydrogen chloride, can, however, be performed more conveniently by the action of hydrogen



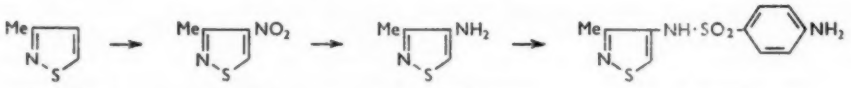
peroxide or persulphates and resembles that of amidinothioureas.[3] The amine (XVIII) was a useful intermediate for the preparation of many derivatives. Direct nitration gave the nitramine (XXVII), but the acetyl (XXIVa) and the dichloroacetyl (XXIVb) derivative under similar conditions gave the 4-nitro-compounds (XXVa) and (XXVb). Each



of these gave 5-amino-3-methyl-4-nitroisothiazole (XXII) on hydrolysis. This was converted by the Sandmeyer reaction into 5-bromo-3-methyl-4-nitroisothiazole (XXI),

[3] Kurzer, *J.*, 1955, 2288; *J.*, 1956, 2345.

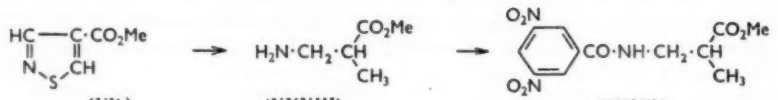
which was also prepared by nitration of 5-bromo-3-methylisothiazole (XX). Treatment of the bromo-compound (XXI) with sodium iodide and acetic acid (reagents used by Blatt and Tristram [4] for the elimination of chlorine from picryl chloride) gave only 5-iodo-3-methyl-4-nitroisothiazole. The bromo-compound (XX) was also degraded, through the nitrile (XIX) and acid (XXIII), to 3-methylisothiazole (XXVI), a substance which closely resembles the parent base in physical properties. The nitrile (XIX) was converted into the corresponding thioamide, and the methyl ester of the acid (XXIII) into the hydrazide. 5-Acetamido-4-amino-3-methylisothiazole (XXIX) and the sulphonamides (XXVIIIa * and b) were also prepared. Nitration of 3-methylisothiazole gave the 4-nitro-derivative (XXX) which was reduced by ferrous sulphate and ammonia to 4-amino-3-methylisothiazole (XXXI), derivatives of which differed from those of the corresponding 5-amino-compound. Catalytic reduction was unsuccessful. The amine (XXXI) was converted into the sulphonamide (XXXII), a position isomer of (XXVIIIa).



(XXVI) (XXX) (XXXI) (XXXII)

We regard the smooth decarboxylation of the 5-acid (XXIII) as compelling evidence for the loss of the 5-carboxy-group from the dicarboxylic acid (IV). Contributory evidence is provided by the following facts:

(a) Reductive desulphurization of the monomethyl ester (VIb) gave an amino-ester (XXXIII), which was converted into a 3,5-dinitrobenzoyl derivative [presumably (XXXIV)]. Kuhn–Roth analysis gave a *C*-methyl figure supporting this structure, whereas desulphurization of methyl isothiazole-5-carboxylate would have given an amino-ester containing no *C*-methyl group.



(VIb) (XXXIII) (XXXIV)

(b) 4-Aminoisothiazole exhibits the expected aromatic properties and was converted into isothiazole by reductive diazotization. 5-Amino-3-methylisothiazole, on the other hand, gave the bromo- and the chloro-compound under normal Sandmeyer conditions, but could not be converted by diazotization into the nitrile or into 3-methylisothiazole. 3-Amino- and 2(or 4)-aminopyridines behave similarly.

Experimental

5-Aminobenz[d]*isothiazole.*—2-Chloro-5-nitrobenzaldehyde was prepared by nitration of *o*-chlorobenzaldehyde.[5] Treatment with ethanolic sodium disulphide gave di-(2-formyl-4-nitrophenyl) disulphide [6] and this was converted into 2-formyl-4-nitrophenylsulphenyl bromide by warming with bromine in carbon tetrachloride.[7] The sulphenyl bromide gave 5-nitrobenz-[*d*]isothiazole when boiled with concentrated aqueous ammonia and benzene,[8] and reduction

* 5-*p*-Aminobenzenesulphonamido-3-methylisothiazole (XXVIIIa) is of considerable interest as an antibacterial agent. It is the subject of B.P. Applns. Nos. 32,801/56, 32,259/57, and 21,628—32,802/56.

[4] Cf. Blatt and Tristram, *J. Amer. Chem. Soc.*, 1952, **74**, 6273.
[5] Erdmann, *Annalen*, 1893, **272**, 153.
[6] Fries and Brothuhn, *Ber.*, 1923, **56**, 1630.
[7] Fries, Eishold, and Vahlberg, *Annalen*, 1927, **454**, 272.
[8] *Idem*, *ibid.*, p. 279.

with ferrous sulphate in ethanol and aqueous ammonia gave 5-aminobenz[d]isothiazole.[8] The overall yield was about 25%.

Isothiazole-4,5-dicarboxylic Acid (IV).—To a suspension of finely powdered 5-aminobenz[*d*]-isothiazole (47·4 g.) in stirred, boiling water (1260 c.c.) and potassium carbonate (630 g.) was slowly added a solution of potassium permanganate (300 g.) in hot water (3150 c.c.). Decolorization was immediate at the beginning of the addition but slowed considerably towards the end. Boiling was continued for 2 hr. and the mixture was then cooled and filtered. The filtrate and aqueous washings were treated with concentrated hydrochloric acid to pH 1 and were continuously extracted with ether (1 l.) for 48 hr. Evaporation of the dried ($MgSO_4$) extracts gave the crude dicarboxylic acid (41·0 g.). This was dissolved in water (100 c.c.), and the solution was filtered from a little sticky residue and treated with 2N-sodium hydroxide to pH 4. After several hours, the *monosodium salt* was collected and the filtrate saturated with sodium chloride [total yield, 31·5 g.; m. p. 262° (decomp.)]. Recrystallization from water gave colourless hydrated needles, m. p. 275° (decomp.) (Found: N, 6·4; S, 15·2; Na, 10·8; loss in wt. at 100°, 8·6. $C_5H_2O_4NSNa,H_2O$ requires N, 6·6; S, 15·0; Na, 10·8; loss at 100°, 8·45%).

The free acid could not be obtained by acidification of an aqueous solution of the sodium salt, nor by boiling it with 2N-sulphuric acid; in each case it was recovered unchanged. The salt (31 g.) was dissolved in 2N-sulphuric acid (800 c.c.), and the solution was continuously extracted with ether (500 c.c.) overnight. Evaporation of the dried ($MgSO_4$) extracts gave *isothiazole-4,5-dicarboxylic acid* (23·8 g.), m. p. 144° (decomp.). Crystallization from benzene gave colourless prisms, m. p. 145° (decomp.) (Found: C, 35·0; H, 2·0; N, 8·0; S, 18·7. $C_5H_3O_4NS$ requires C, 34·7; H, 1·7; N, 8·1; S, 18·5%).

Isothiazole-4-carboxylic Acid (V).—Isothiazole-4,5-dicarboxylic acid (40·8 g.) was boiled under reflux with mesitylene (400 c.c.) for 2 hr. The hot solution was filtered from a little tar and cooled. *Isothiazole-4-carboxylic acid* (26·1 g.; m. p. 161—162°) was collected, washed with benzene, and dried. Recrystallization from water gave colourless needles, m. p. 162° (Found: C, 37·5; H, 2·2; N, 10·8; S, 24·75. $C_4H_3O_2NS$ requires C, 37·2; H, 2·3; N, 10·85; S, 24·8%).

Methyl Isothiazole-4-carboxylate (VIb).—Isothiazole-4-carboxylic acid (26·1 g.) was slowly added to an ethereal (750 c.c.) solution of diazomethane prepared from methylnitrosourea (75 g.). After 12 hr., evaporation gave the *methyl ester* (28·6 g.), which solidified. Recrystallization from light petroleum (b. p. 40—60°) gave colourless needles, m. p. 55° (Found: C, 42·0; H, 3·8; N, 10·0. $C_5H_5O_2NS$ requires C, 41·95; H, 3·5; N, 9·8%).

Isothiazole-4-carboxyhydrazide (VIc).—Hydrazine hydrate (100%; 13 c.c.) was added to methyl isothiazole-4-carboxylate (13 g.) in ethanol (60 c.c.), and the mixture was heated on the steam-bath for 30 min. before being cooled overnight. The *isothiazole-4-carboxyhydrazide* (11·5 g., m. p. 173—175°) recrystallized from water in straw-coloured prisms, m. p. 176° (decomp.) (Found: C, 33·6; H, 3·4; N, 29·5; S, 22·85. $C_4H_5ON_3S$ requires C, 33·6; H, 3·5; N, 29·4; S, 22·4%).

Isothiazole-4-carboxyazide (VId).—A suspension of the hydrazide (17·0 g.) in concentrated hydrochloric acid (85 c.c.) and water (85 c.c.) was covered with ether (265 c.c.) and stirred vigorously at −5° to 0° while being treated with sodium nitrite (14·4 g.) in water (58 c.c.). The ethereal layer was separated after 2—3 hr. and the aqueous layer was re-extracted with ether (2 × 200 c.c.). The combined ethereal liquors were washed with aqueous sodium hydrogen carbonate and with water, dried ($CaSO_4$), and evaporated. The residual *azide* (15·4 g.) crystallized from light petroleum (b. p. 40—60°) in colourless prisms, m. p. 32° (Found: C, 31·2; H, 1·5; N, 36·5. $C_4H_3ON_4S$ requires C, 31·2; H, 1·3; N, 36·3%).

4-Phthalimidoisothiazole (VIh).—Isothiazole-4-carboxyazide (8·3 g.) and phthalic anhydride (8·0 g.) were heated on the steam-bath with dry pyridine (60 c.c.) for 3 hr. The solvent was removed under reduced pressure and the solid residue dissolved in the minimum quantity of boiling ethanol. *4-Phthalimidoisothiazole* separated on cooling (5·1 g.; m. p. 155—156°) and recrystallized from light petroleum (b. p. 80—100°) as needles, m. p. 157° (Found: C, 57·05; H, 3·0; N, 11·9. $C_{11}H_6O_2N_2S$ requires C, 57·4; H, 2·6; N, 12·2%). Occasionally the product was mixed with an ethanol-insoluble compound which crystallized from pyridine in colourless prisms, m. p. 294—295°. This was probably *4-isothiazolyl isocyanate trimer* (Found: C, 37·95; H, 1·2; N, 21·95; S, 24·8%; *M*, 370. $C_{15}H_6O_3N_6S_3$ requires C, 38·1; H, 1·6; N, 22·2; S, 25·4%; *M*, 378).

4-Ethoxycarbonylaminoisothiazole (VIg).—A solution of isothiazole-4-carboxyazide (4·2 g.) in dry ethanol (120 c.c.) was boiled under reflux for 3 hr. The solvent was removed under

reduced pressure to give 4-*ethoxycarbonylaminoisothiazole* (4·0 g.; m. p. 72—74°), in colourless prisms, m. p. 78° [from light petroleum (b. p. 60—80°)] (Found: C, 41·7; H, 5·1; N, 16·1. $C_6H_8O_2N_2S$ requires C, 41·9; H, 4·7; N, 16·3%).

4-*Benzyloxycarbonylaminoisothiazole* (VIe).—Isothiazole-4-carboxyazide (39·0 g.) was heated with benzyl alcohol (500 c.c.) for 1 hr. at 150°. The solvent was removed under reduced pressure to give oily 4-*benzyloxycarbonylaminoisothiazole* which solidified (54·3 g.; m. p. 99—100°) after trituration with light petroleum (b. p. 80—100°). Recrystallization from light petroleum (b. p. 80—100°) gave colourless needles, m. p. 101° (Found: C, 56·7; H, 4·5; N, 12·1. $C_{11}H_{10}O_2N_2S$ requires C, 56·4; H, 4·3; N, 12·0%).

4-*Aminoisothiazole* (VIf).—*Method* I. Hydrazine hydrate (100%; 2·6 g., 2 mol.) in a little ethanol was added to a stirred suspension of finely powdered 4-phthalimidoisothiazole (6·0 g.) in ethanol (100 c.c.). After 18 hr., the white flocculent precipitate [5·0 g.; m. p. 165° (decomp.)] was collected, washed with a little ethanol, and dried. The powdered product was stirred with 2N-hydrochloric acid (100 c.c.), and the solution filtered from phthalhydrazide [3·0 g.; m. p 340° (decomp.)]. The filtrate was evaporated to small bulk, made alkaline with 2N-sodium hydroxide, and continuously extracted with ether for 18 hr. Evaporation of the dried ($MgSO_4$) extracts gave an oil (1·2 g.) which solidified. Crystallization from light petroleum (b. p. 40—60°) gave 4-aminoisothiazole in colourless needles, m. p. 45°. The m. p. was not depressed on admixture with a specimen prepared by Method II.

Method II. 4-Benzyloxycarbonylaminoisothiazole (52·0 g.) was treated with 36% w/w hydrogen bromide in acetic acid (500 c.c.) and set aside at room temperature for 1 hr. After 1 hr. on the steam-bath the product (54·7 g.), consisting mainly of the amine dihydrobromide, was collected, washed with acetic acid, and dried. This salt was dissolved in water (60 c.c.), and the solution made alkaline with sodium carbonate and continuously extracted with ether (75 c.c.) for 18 hr. Evaporation of the dried extracts gave 4-*aminoisothiazole* (22·2 g.) as pale yellow needles, m. p. 35—40°. Recrystallization from light petroleum (b. p. 40—60°) gave colourless needles, m. p. and mixed m. p. 45° (Found: C, 36·2; H, 4·0; N, 27·7. $C_3H_4N_2S$ requires C, 36·0; H, 4·0; N, 28·0%).

The *acetyl* derivative crystallized from water in colourless prisms, m. p. 127—128° (Found: C, 42·05; H, 4·4; N, 19·7. $C_5H_6ON_2S$ requires C, 42·2; H, 4·25; N, 19·7%). The *benzoyl* derivative crystallized from aqueous ethanol in colourless needles, m. p. 137° (Found: C, 58·8; H, 3·9. $C_{10}H_8ON_2S$ requires C, 58·8; H, 3·95%).

4-p-*Acetamidobenzenesulphonamidoisothiazole*.—To an ice-cooled solution of 4-aminoisothiazole (12·5 g.) in dry pyridine (125 c.c.) was slowly added, below 10°, *p*-acetamidobenzenesulphonyl chloride (32·0 g.). After 18 hr. at room temperature, the solution was stirred into water (4 l.), and the solid product was filtered off, washed with water, and dried (37·0 g.; m. p. 257—258°). Recrystallization from ethanol gave 4-p-*acetamidobenzenesulphonamidoisothiazole* in fawn needles, m. p. 261—262° (Found: C, 44·8; H, 4·0; N, 14·4; S, 21·15. $C_{11}H_{11}O_3N_3S_2$ requires C, 44·3; H, 3·7; N, 14·1; S, 21·6%).

4-p-*Aminobenzenesulphonamidoisothiazole* (VIj).—A solution of 4-*p*-acetamidobenzenesulphonamidoisothiazole (37·5 g.) in 2N-sodium hydroxide (300 c.c.) was boiled for 2 hr., and for a further 5 min. after the addition of decolorizing charcoal (1 g.). The cold, filtered solution was treated with concentrated hydrochloric acid to pH 6, 4-p-*aminobenzenesulphonamidoisothiazole* (30·1 g.; m. p. 195—200°) being collected, washed with water, and dried. Recrystallization from ethanol gave colourless needles, m. p. 203—204° (Found: C, 42·25; H, 3·7; N, 16·2; S, 25·2. $C_9H_9O_2N_3S$ requires C, 42·35; H, 3·55; N, 16·5; S, 25·1%). The same compound was obtained in 89% yield by hydrolysis of the acetyl derivative with 2N-hydrochloric acid.

Isothiazole (1,2-*Thiazole*) (VIk).—A solution of 4-aminoisothiazole (10·0 g.) in concentrated hydrochloric acid (40 c.c.) and water (40 c.c.) was treated at 0—5° with an ice-cooled solution of sodium nitrite (8·1 g.) in water (40 c.c.). Ice-cooled 30—32% w/w hypophosphorous acid (260 c.c.) was added, and the mixture was stirred at 0° for 30 min. and then set aside at 0° for 36 hr. The solution was then made alkaline with 50% sodium hydroxide solution and filtered, and the filtrate steam-distilled into ether (100 c.c.) until the distillate no longer gave a crystalline precipitate with mercuric chloride solution. The ether layer was separated and the aqueous layer extracted with ether (5 × 100 c.c.). Evaporation of the dried ($CaSO_4$) combined ethereal liquors gave *isothiazole* (4·4 g.). Distillation gave a colourless liquid (2·9 g.), b.p. 113°/770 mm. (Found: C, 42·3; H, 3·7; N, 16·55; S, 37·8. C_3H_3NS requires C, 42·3; H, 3·55; N, 16·5;

S, 37·7%). Isothiazole is a colourless, highly refractive (n_D^{20} 1·5320), mobile liquid with a pyridine- and thiazole-like odour and $\lambda_{max.}$ 242 mμ (log ε 3·818). It is soluble in water and in ether, and gives crystalline derivatives with metallic salts. The *mercurichloride* forms unstable colourless needles, m. p. 173° (decomp.; bath preheated to 170°) (Found: N, 3·9; S, 9·1. $C_3H_3NS,HgCl_2$ requires N, 3·9; S, 9·0%). The chloroplatinate separates in yellow prisms, decomp., 360—370°. A satisfactory analysis could not be obtained (Found: C, 11·7; H, 2·0; N, 5·8; S, 10·6; Pt, 32·1. Calc. for $2C_3H_3NS,H_2PtCl_6$: C, 12·4; H, 1·4; N, 4·8; S, 11·1; Pt, 33·6%). The *chloroaurate* forms golden needles, melting by 250° (decomp.) before resolidifying (Found: C, 8·5; H, 1·1; N, 3·3; S, 7·5; Au, 45·8. $C_3H_3NS,HAuCl_4$ requires C, 8·5; H, 0·95; N, 3·3; S, 7·5; Au, 46·35%).

Isothiazole-4-carboxyamide (VIa).—Isothiazole-4-carboxylic acid (3·1 g.) was boiled with thionyl chloride (30 c.c.) until a clear solution was obtained, then the solvent was removed under reduced pressure. The residual acid chloride in dry ether (25 c.c.) gave, with aqueous ammonia (*d* 0·88; 10 c.c.), *isothiazole-4-carboxyamide* (2·5 g.; m. p. 183—188°), crystallizing from water in prisms, m. p. 192—193° (Found: C, 37·3; H, 3·2; N, 21·3. $C_4H_4ON_2S$ requires C, 37·5; H, 3·15; N, 21·9%).

Diethyl Isothiazole-4,5-dicarboxylate (X).—The dicarboxylic acid (8·4 g.) was boiled under reflux with thionyl chloride (50 c.c.) for 90 min. The dichloride (8·8 g.), b. p. 122—124°/10 mm., and dry ethanol (50 c.c.) were boiled under reflux for 30 min. to give the pale yellow *diethyl ester* (7·8 g.), b. p. 154°/15 mm. (Found: C, 47·3; H, 5·0; N, 6·1. $C_9H_{11}O_4NS$ requires C, 47·15; H, 4·8; N, 6·1%). The dichloride was also conveniently obtained from the monosodium salt and thionyl chloride.

4-Ethoxycarbonylisothiazole-5-carboxylic Acid (XIa).—*Method* I. The diethyl ester (3·1 g.) at −5° to −10° was treated dropwise during 1 hr. with ethanolic N-potassium hydroxide (6·8 c.c.). The precipitated potassium salt (1·1 g.; m. p. 145—153°) was collected and addition of dry ether to the filtrate gave a further 0·15 g., m. p. 137—145°. This was filtered off, ether was removed from the filtrate, and the alcoholic residue was again treated with ethanolic N-potassium hydroxide (6·8 c.c.) to give further potassium salt (1·15 g.; m. p. 162—165°; and 0·15 g., m. p. 157—160°). The combined salts (2·55 g.) were dissolved in a little water, and the solution was acidified with hydrochloric acid to give *4-ethoxycarbonylisothiazole-5-carboxylic acid* (1·2 g.; m. p. 80—83°). Crystallization from light petroleum (b. p. 40—60°) gave colourless plates, m. p. 83—84° (Found: C, 42·2; H, 3·9; N, 6·8. $C_7H_7O_4NS$ requires C, 41·8; H, 3·5; N, 7·0%). The acid was decarboxylated at 140°. The residual oil, dissolved in ethanol and treated with hydrazine hydrate, was converted into the hydrazide, m. p. 174—175°, undepressed on admixture with a specimen prepared from methyl isothiazole-4-carboxylate.

Method II.—The dicarboxylic acid (2·0 g.) in water (30 c.c.) and 0·8N-ammonia (14·45 c.c.; 1 mol.) was treated with N-silver nitrate (11·6 c.c.; 1 mol.). The silver salt was collected, washed, dried *in vacuo* (2·95 g.), powdered, and boiled under reflux with chloroform (50 c.c.) and ethyl iodide (2·5 g.) for 7 hr. The mixture was filtered, and the filtrate evaporated on the steam-bath to constant weight. The cooled residual oil partially crystallized on being seeded with 4-ethoxycarbonylisothiazole-5-carboxylic acid. The product (0·35 g.) separated from light petroleum (b. p. 40—60°) in colourless plates, m. p. 80—82°, not depressed on admixture with this half-ester. The remaining oil, dissolved in a little 2N-sodium hydroxide and treated with 2N-hydrochloric acid, gave the monosodium salt (0·45 g.), in needles, m. p. 270° (decomp.).

5-Carboxyisothiazole-4-carboxyamide (XIb).—A solution of 4-ethoxycarbonylisothiazole-5-carboxylic acid (0·55 g.) in aqueous ammonia (*d* 0·88; 10 c.c.) was set aside overnight. Acidification of an aqueous solution of the crystalline product gave *5-carboxyisothiazole-4-carboxyamide* [0·35 g.; m. p. 175° (decomp.)] which recrystallized from water in colourless needles, m. p. 175° with decarboxylation, followed by resolidification to isothiazole-4-carboxyamide, m. p. 192° (Found: C, 35·2; H, 2·3; N, 16·0. $C_5H_4O_3N_2S$ requires C, 34·9; H, 2·3; N, 16·3%).

Isothiazole-4,5-dicarboxyamide (XIII).—Isothiazole-4,5-dicarbonyl chloride (0·6 g.) was added to aqueous ammonia (*d* 0·88; 1 c.c.). The precipitated *isothiazole-4,5-dicarboxyamide* crystallized from water in needles, m. p. 243° (Found: C, 35·2; H, 3·1; N, 24·8. $C_5H_5O_2N_3S$ requires C, 35·1; H, 2·9; N, 24·6%).

4,5,6,7-Tetrahydro-4,7-dioxopyridazino[4,5-d]*isothiazole* (XIV).—Diethyl isothiazole-4,5-dicarboxylate (2·8 g.), methanol (5 c.c.), and 100% hydrazine hydrate (1·85 g.) were warmed on the steam-bath for 30 min. The yellow product (1·75 g., m. p. 220° decomp.) was collected

XUM

after 12 hr., washed with water, and stirred with 2N-hydrochloric acid (20 c.c.). The resulting *hydrazide* (1·04 g.) crystallized from water in colourless needles, m. p. 320° (decomp.) (Found: C, 35·75; H, 2·0; N, 24·7. $C_5H_3O_3N_3S$ requires C, 35·5; H, 1·8; N, 24·8%).

Isothiazole-4,5-dicarboxylic Anhydride (VIII).—The dicarbonyl chloride (IX) (10 g.) was boiled for 18 hr. with yellow mercuric oxide (10·5 g.) and dry benzene (75 c.c.). The cooled mixture was filtered and the residue extracted with boiling benzene (50 c.c.). The filtrate and extract were evaporated under reduced pressure; the residue was crystallized from light petroleum (b. p. 60—80°). The product (4·7 g.; m. p. 100—115°) consisted of the anhydride contaminated with a little mercuric chloride. Repeated recrystallization from light petroleum (b. p. 60—80°) gave the pure anhydride in prisms, m. p. 118—120°. Satisfactory analytical results could not be obtained, since the anhydride rapidly absorbed water (Found: C, 38·15; H, 1·2; N, 9·1. Calc. for C_5HO_3NS: C, 38·7; H, 0·65; N, 9·0%).

4-Carboxyisothiazole-5-carboxyamide (XIIb).—*Method* I. Isothiazole-4,5-dicarboxylic anhydride (12·0 g.) and aqueous ammonia (*d* 0·88; 100 c.c.) were warmed on the steam-bath until most of the excess of ammonia had been removed. Acidification with hydrochloric acid to pH 1 gave the crude *amide* (9·0 g.), m. p. 170—245° (decomp.); when pure it formed needles, m. p. 248—251° (decomp.) after repeated recrystallization from water (Found: C, 34·9; H, 2·4; N, 16·0. $C_5H_4O_3N_2S$ requires C, 34·9; H, 2·3; N, 16·3%).

Method II. The anhydride (2·0 g.) in dry ethanol (20 c.c.) was boiled under reflux for 1 hr., the solvent was removed, and the crude 5-ethoxycarbonylisothiazole-4-carboxylic acid (2·0 g.) was dissolved in aqueous ammonia (*d* 0·88; 25 c.c.). After 12 hr., excess of ammonia was removed at 100° and the solution, on acidification with hydrochloric acid, gave 4-carboxyisothiazole-5-carboxyamide (1·0 g.), m. p. 241—243°. Recrystallization from water gave colourless needles, m. p. and mixed m. p. 248—250° (decomp.).

Desulphurization of Methyl Isothiazole-4-carboxylate.—Methyl isothiazole-4-carboxylate (5·0 g.), Raney nickel (25 g.), and methanol (150 c.c.) were boiled under reflux for 6 hr. The spent sludge was removed and the residual solution boiled with decolorizing charcoal and filtered (Hyflo). Evaporation of the filtrate gave a brown syrup which contained nitrogen but no sulphur. It was readily soluble in 2N-hydrochloric acid, less so in 2N-sodium hydroxide, did not react with aqueous sodium hydrogen carbonate, but slowly gave a crystalline precipitate with chloroplatinic acid. The syrup was triturated with ether, and the solution filtered from a sticky residue. Evaporation of the filtrate gave a gum (0·5 g.) which was dissolved in dry pyridine (5 c.c.) and treated with 3,5-dinitrobenzoyl chloride (2·5 g.) in dry pyridine (50 c.c.). After 18 hr., the solution was poured into water (250 c.c.), and the emulsion was washed with water, 2N-hydrochloric acid, water, sodium hydrogen carbonate, and water. Evaporation of the dried ($MgSO_4$) ethereal liquors left a thick syrup which yielded pale yellow crystals (0·3 g., m. p. 193—199°) on trituration with chloroform. Recrystallization from chloroform gave *methyl β-3,5-dinitrobenzamido-α-methylpropionate*, m. p. 201—202° (Found: C, 46·9; H, 3·8; N, 13·5; MeO, 10·2; *C*-Me, 4·5%; *M*, 270. $C_{12}H_{13}O_7N_3$ requires C, 46·3; H, 4·2; N, 13·5; MeO, 10·0; *C*-Me, 4·8%; *M*, 311).

β-Iminothiobutyramide (XVII).—Dry hydrogen sulphide (15—20 l./hr.) was passed through a 2·5 cm. diameter, grade 2, sintered-glass bubbler into a solution of β-iminobutyronitrile (1 kg.) in dry pyridine (3 l.) for 8 hr. at 35—40°. The reaction flask was stoppered overnight, and the solution was again treated with hydrogen sulphide for 8 hr. and set aside for a second night. The pyridine was removed on the steam-bath under reduced pressure and the residual oil set aside to crystallize. The product was triturated with ether, collected, washed with ether, and dried (683 g.; m. p. 141—142°). The ether washings were concentrated, the residue was dissolved in dry pyridine (2 l.), and the solution treated with hydrogen sulphide as before to give further product (479 g.; m. p. 124—128°) which, crystallized from chloroform, had m. p. 138—141° (244 g.). Recrystallization from benzene or chloroform gave *β-iminothiobutyramide* in yellow needles, m. p. 142° (Found: C, 41·2; H, 7·1; N, 23·9; S, 27·8. $C_4H_8N_2S$ requires C, 41·3; H, 6·9; N, 24·1; S, 27·6%).

5-Amino-3-methylisothiazole (XVIII).—*Method* I. An aqueous solution of chloramine was prepared by treating sodium hydroxide (63·0 g.) in water (300 c.c.) and ice (350 g.) with chlorine (48·7 g.), and stirring the resulting solution into aqueous ammonia (*d* 0·88; 72·0 c.c.), water (1 l.), and ice (1 kg.). Powdered β-iminothiobutyramide (80·0 g.) was added, and the mixture was stirred for 6 hr. and set aside overnight. Solids were filtered off, and the filtrate was continuously extracted with ether (1 l.) for 18 hr. The dried ($MgSO_4$) extracts were treated

with dry hydrogen chloride for 1 hr., and the *hydrochloride* (67·0 g.) collected, washed with ether, and dried for 1 hr. at 40°. Crystallization from ethanol–ether gave colourless needles, m. p. *ca.* 240° (decomp.) (Found: C, 32·2; H, 4·85; N, 18·8; Cl, 23·55; S, 21·2. $C_4H_6N_2S$,HCl requires C, 31·9; H, 4·7; N, 18·6; Cl, 23·5; S, 21·3%). The hydrochloride (67·0 g.) was dissolved in water (670 c.c.), and the solution filtered from a little flocculent residue, treated with 50% sodium hydroxide solution (67 c.c.), and continuously extracted with ether (250 c.c.) for 18 hr. Evaporation of the dried ($MgSO_4$) extracts gave crude *5-amino-3-methylisothiazole* (34·0 g.); distillation gave material (29·0 g.), b. p. 100—105°/0·3 mm., pale yellow prisms, m. p. 48—49°. Recrystallization from light petroleum (b. p. 40—60°) gave colourless prisms, m. p. 52—53° (Found: C, 41·9; H, 5·4; N, 24·2. $C_4H_6N_2S$ requires C, 42·1; H, 5·3; N, 24·5%).

Several by-products, not yet identified, were isolated from time to time. These substances are in the annexed Table.

Sub-stance	M. p.	Formula	Found (%) C	H	N	S	Required (%) C	H	N	S
(*a*)	191—192° (decomp.)	$C_4H_5ON_3S$	33·9	3·6	29·55	22·2	33·6	3·5	29·4	22·4
(*b*)	231	$C_8H_8N_2$	65·5	6·3	28·0		65·3	6·2	28·55	
(*c*)	300—301	$C_{16}H_{14}N_4S,0·5H_2O$	63·5	5·05	18·85	9·9	63·0	4·95	18·4	10·5
(*d*)	305—307	$C_{16}H_{16}O_2N_4$	65·0	5·7	19·7	Nil	65·0	5·4	18·9	
(*e*)	228—229 (decomp.)	$C_8H_{10}ON_2S,HCl,1·7H_2O$ *	38·6	5·7	10·7	12·6	38·4	5·9	11·2	12·8
(*f*)	117—125									

* Found: Cl, 13·5; H_2O, 12·35. Required: Cl, 14·2; H_2O, 12·4%.

(*a*) Reaction residue. (*b*) Reaction residue, with S. (*c*) Separated from first ether extracts. (*d*) From (*c*), by repeated recrystn. from EtOH. (*e*) Pptd. from first ether extracts by prolonged treatment with HCl. (*f*) From first ether extracts by extraction with 2N-NaOH.

The *amine picrate* crystallized from ethanol in needles, decomp. from 185° (Found: C, 35·3; H, 2·9; N, 20·25. $C_4H_6N_2S,C_6H_3O_7N_3$ requires C, 35·0; H, 2·65; N, 20·4%). The *acetyl derivative*, from the base and acetic anhydride, crystallized from water in needles, m. p. 180—181° (Found: C, 45·9; H, 5·2; N, 17·4. $C_6H_8ON_2S$ requires C, 46·1; H, 5·2; N, 17·9%). The *dichloroacetyl* derivative, from the amine and dichloroacetyl chloride in ether, crystallized from ethyl acetate–light petroleum (b. p. 60—80°) in needles, m. p. 189—190° (Found: N, 12·5; Cl, 31·5. $C_6H_6ON_2Cl_2S$ requires N, 12·45; Cl, 31·5%). The *benzoyl derivative*, from the amine and alkaline benzoyl chloride, separated from aqueous alcohol in needles, m. p. 222—223° (Found: C, 60·8; H, 4·7; N, 12·9; S, 15·2. $C_{11}H_{10}ON_2S$ requires C, 60·5; H, 4·6; N, 12·8; S, 14·7%).

Method II. To a solution of ammonium persulphate (780 g.) and sodium hydroxide (272 g.) in water (8·5 l.) at 15°, powdered β-iminothiobutyramide (394 g.) was added, with continued stirring, during 30 min., the temperature being kept at 15—20° by the addition of ice (*ca.* 3·5 kg.); aqueous ammonia (*d* 0·88) was added as necessary (*ca.* 200 c.c.) to maintain the pH at >9. After 1 hr., the thioamide had dissolved to give a clear, wine-red solution. The solution was stirred for a further 4 hr. and was set aside overnight. It was then filtered and the filtrate treated as described in Method I.* Distilled amine was obtained in 36% yield.

3-Methyl-5-nitraminoisothiazole (XXVII).—A solution of 5-amino-3-methylisothiazole (10 g.) in concentrated sulphuric acid (25 c.c.) was slowly treated with fuming nitric acid (*d* 1·51; 5 c.c.) below 40°. After 16 hr., the clear yellow solution was stirred with ice (500 g.), and the precipitated *3-methyl-5-nitraminoisothiazole* [13·9 g.; m. p. 193° (decomp.)] was collected, washed with water, and dried. Recrystallization from ethanol gave pale yellow needles, m. p. 200—201° (Found: N, 26·4. $C_4H_5O_2N_3S$ requires N, 26·4%).

5-Dichloroacetamido-3-methyl-4-nitroisothiazole (XXVb).—Fuming nitric acid (*d* 1·51; 4·7 c.c.) was added dropwise, with stirring, to 5-dichloroacetamido-3-methylisothiazole (21·0 g.) in concentrated sulphuric acid (63 c.c.) at <5°. The mixture was allowed to reach room temperature and was set aside overnight. Treatment with ice (200 g.) and water (1 l.) gave *5-dichloroacetamido-3-methyl-4-nitroisothiazole* (24·4 g.) as a white solid, m. p. 91—92°. Crystallization from light petroleum (b. p. 60—80°) gave fluffy white needles, m. p. 91—92° (Found: N, 15·7; Cl, 26·1. $C_6H_5O_3N_3Cl_2S$ requires N, 15·6; Cl, 26·25%).

5-Acetamido-3-methyl-4-nitroisothiazole (XXVa) was similarly prepared (90% yield) from

* No second hydrochloride was obtained, nor were any by-products noted.

5-acetamido-3-methylisothiazole and crystallized from alcohol in plates, m. p. 187° (Found: C, 35·85; H, 3·5; N, 20·95. $C_6H_7O_3N_3S$ requires C, 35·8; H, 3·5; N, 20·9%).

5-Amino-3-methyl-4-nitroisothiazole (XXII).—5-Dichloroacetamido-3-methyl-4-nitroisothiazole (19·0 g.) was boiled with 4N-hydrochloric acid (190 c.c.) until dissolution was complete (1 hr.). Hot water (190 c.c.) and charcoal (1 g.) were added, boiling was continued for 5 min., and the hot solution was filtered. *5-Amino-3-methyl-4-nitroisothiazole* (7·8 g.) separated as pale yellow prisms, m. p. 185—186°, unchanged by recrystallization from ethanol (Found: C, 30·3; H, 3·23; N, 26·15. $C_4H_5O_2N_3S$ requires C, 30·2; H, 3·2; N, 26·4%). The amine was also obtained (80% yield) in a similar manner from 5-acetamido-3-methyl-4-nitroisothiazole.

5-Acetamido-4-amino-3-methylisothiazole (XXIX).—A suspension of 5-acetamido-3-methyl-4-nitroisothiazole (40·0 g.) and platinum oxide catalyst (2·0 g.) in ethanol (350 c.c.) was reduced with hydrogen at 66° under a pressure of 300 lb./sq. in. Uptake was complete in 4 hr. Hydrated *5-acetamido-4-amino-3-methylisothiazole* (30·0 g.; m. p. 222—223°) crystallized from water in colourless needles, m. p. 225—226° (Found: C, 38·3; H, 6·0; N, 21·6; H_2O, 9·7. $C_6H_9ON_3S,H_2O$ requires C, 38·1; H, 5·9; N, 22·2; H_2O, 9·5%).

5-p-Acetamidobenzenesulphonamido-3-methylisothiazole.—A solution of *p*-acetamidobenzenesulphonyl chloride (130 g.) in dry pyridine (225 c.c.) was added, with stirring, to a solution of 5-amino-3-methylisothiazole (57 g.) in dry pyridine (225 c.c.). The temperature rose to 50—60°, and the mixture was then heated at 90—95° for 30 min. The mixture was cooled and stirred into 2N-hydrochloric acid (5·5 l.) and ice (1 kg.). After 30 min., the solid product was collected, washed with water, and drained. It was then stirred with 2N-ammonia (1·5 l.) for 30 min., insoluble material was removed, and the filtrate was stirred while 2N-acetic acid was added to bring the pH to 7·4. A small amount of highly coloured impurity was removed, and the filtrate stirred with charcoal (10 g.) for 1 hr. and treated with 2N-hydrochloric acid to pH 1. *5-p-Acetamidobenzenesulphonamido-3-methylisothiazole* separated as a pale yellow powder (83·5 g.), m. p. 265—268°. Crystallization from acetic acid gave straw-coloured, lenticular crystals, m. p. 271·5—272·5° (Found: C, 45·6; H, 4·2; N, 12·9. $C_{12}H_{13}O_3N_3S_2$ requires C, 46·3; H, 4·2; N, 13·5%).

5-p-Aminobenzenesulphonamido-3-methylisothiazole (XXVIIIa).—5-*p*-Acetamidobenzenesulphonamido-3-methylisothiazole (107 g.) was added to boiling 2N-sodium hydroxide (1070 c.c.), boiling was continued for 30 min. and then for a further 10 min. after the addition of decolorizing charcoal (6 g.). The cooled, filtered solution was stirred and treated with sulphur dioxide to pH 4—5. The precipitated *5-p-aminobenzenesulphonamido-3-methylisothiazole* (78 g.; m. p. 186—189°) was purified by dissolution in water containing the minimum of ammonia, treatment with charcoal, and reprecipitation with acetic acid at pH 4—5 (72 g.; m. p. 189—191°). Recrystallization from water gave the sulphonamide in cream needles, m. p. 192—192·5° (Found: C, 44·9; H, 4·3; N, 15·7; S, 24·1. $C_{10}H_{11}O_2N_3S_2$ requires C, 44·6; H, 4·1; N, 15·6; S, 23·8%). The *sodium derivative* separated from ethanol–ether as pale cream needles, m. p. 345° (decomp.), which absorbed moisture to give the stable hydrate (Found: N, 13·8; Na, 7·35; H_2O, 6·2. $C_{10}H_{10}O_2N_3S_2Na,H_2O$ requires N, 13·6; Na, 7·4; H_2O, 5·8%). The N^4-*succinamido-derivative hemihydrate* was precipitated from 0·5N-aqueous ammonia by the addition of 2N-hydrochloric acid, as a white powder, m. p. 228—229° (Found: C, 44·3; H, 4·1; N, 11·1; H_2O, 2·2. $C_{14}H_{15}O_5N_3S_2,O{\cdot}5H_2O$ requires C, 44·4; H, 4·3; N, 11·1; H_2O, 2·4), and the N^4-*phthalamido-derivative* similarly, m. p. 201—202° (Found: C, 51·9; H, 3·8; N, 10·3. $C_{18}H_{15}O_5N_3S_2$ requires C, 51·8; H, 3·6; N, 10·1%).

5-p-Nitrobenzenesulphonamido-3-methylisothiazole (XXVIIIb) was prepared in only 6% yield in a manner analogous to that described for the *p*-acetamido-derivative. It was precipitated from 0·5N-aqueous ammonia, by treatment with 2N-hydrochloric acid, as fine yellow needles, m. p. 218—219° (Found: C, 40·2; H, 3·2; N, 14·0; S, 21·1. $C_{10}H_9O_4N_3S_2$ requires C, 40·1; H, 3·0; N, 14·0; S, 21·4%).

5-Chloro-3-methylisothiazole.—A solution of 5-amino-3-methylisothiazole (5·7 g.) in 86% phosphoric acid (20 c.c.) was cooled to 5° and treated with concentrated nitric acid (10 c.c.) below 10°. The suspension of nitrate was cooled to 0° and diazotized by cautious addition of sodium nitrite (4·0 g.) in a little water below 5°. After 30 min., the diazotized solution was slowly stirred into a solution of cuprous chloride [prepared in the usual manner from cupric sulphate ($5H_2O$; 15·6 g.), sodium chloride (4·1 g.), and sodium metabisulphite (3·15 g.)] in 50% hydrochloric acid. Evolution of nitrogen was complete in 15 min. The mixture was set

aside overnight, adjusted to pH 4—5 with 2N-sodium hydroxide, and steam-distilled. The distillate (100 c.c.) was extracted with ether (3 × 25 c.c.), and the dried ($MgSO_4$) extracts were concentrated, and distilled at atmospheric pressure (2·1 g.; b. p. 148—155°). Redistillation gave *5-chloro-3-methylisothiazole*, b. p. 154—155°/767 mm. (A satisfactory analysis for chlorine could not be obtained. Found: N, 10·3; Cl, 25·5. C_4H_4NClS requires N, 10·5; Cl, 26·5%.)

5-Bromo-3-methylisothiazole (XX) was prepared in 73% yield in a manner analogous to that described above for the chloro-compound, except that after addition of the diazotized amine solution to cuprous bromide–hydrobromic acid solution it was desirable to leave the cooled mixture for only 1 hr. before dilution and partial neutralization in order to avoid spontaneous decomposition. It distilled as a colourless, mobile liquid, b. p. 72°/13 mm. (Found: N, 8·0; Br, 45·0. C_4H_4NBrS requires N, 7·9; Br, 44·9%).

5-Bromo-3-methyl-4-nitroisothiazole (XXI).—*Method* I. 5-Amino-3-methyl-4-nitroisothiazole (7·85 g.) was diazotized as described for 5-amino-3-methylisothiazole, and the solution was added to one of cuprous bromide and hydrobromic acid prepared from cupric sulphate (15·4 g.). After 1 hr. at 0—5°, the mixture was diluted with an equal volume of water, adjusted to pH 4—5 with 50% sodium hydroxide, and steam-distilled. The distillate was extracted with ether (3 × 50 c.c.), and the dried ($MgSO_4$) extracts were evaporated to give *5-bromo-3-methyl-4-nitroisothiazole* (7·25 g.). Recrystallization from ethanol gave pale yellow needles, m. p. 77—78° (Found: N, 12·45; Br, 35·4. $C_4H_3O_2N_2BrS$ requires N, 12·6; Br, 35·8%).

Method II. A solution of 5-bromo-3-methylisothiazole (3·0 g.) in concentrated sulphuric acid (10 c.c.) was treated with fuming nitric acid (*d* 1·51; 1·0 c.c.), then heated at 115° for 2 hr. The cooled mixture was stirred with ice (100 g.), and the solid product (2·8 g.; m. p. 76—78°) collected, washed with water, and dried. Crystallization from ethanol gave pale yellow needles, m. p. and mixed m. p. 77—78°.

5-Iodo-3-methyl-4-nitroisothiazole.—5-Bromo-3-methyl-4-nitroisothiazole (1·9 g.) and sodium iodide (3·2 g.) were heated in acetone (16·5 c.c.) and acetic acid (1·1 c.c.) for 2 hr. at 100°, then set aside for 16 hr. at room temperature. Solids were filtered off and the filtrate was treated with sodium pyrosulphite (1·07 g.) in water (68 c.c.), to give *5-iodo-3-methyl-4-nitroisothiazole* (1·6 g.; m. p. 94—109°). Recrystallization from light petroleum (b. p. 60—80°) gave pale yellow plates, m. p. 120—121° [Found: C, 17·4; H, 1·3; N, 9·9; I (specific), 46·9; S, 12·05. $C_4H_3O_2N_2IS$ requires C, 17·8; H, 1·1; N, 10·4; I, 47·0; S, 11·9%).

5-Cyano-3-methylisothiazole (XI).—5-Bromo-3-methylisothiazole (10·0 g.) was heated with cuprous cyanide (7·5 g.) at 160° for 3 hr. Distillation gave *5-cyano-3-methylisothiazole* (6·3 g.), b. p. 90—100°/20 mm., m. p. 38—40°. Recrystallization from light petroleum (b. p. 60—80°) gave colourless prisms, m. p. 39—40° (Found: C, 48·0; H, 3·25; N, 22·3. $C_5H_4N_2S$ requires C, 48·4; H, 3·25; N, 22·3%).

3-Methylisothiazole-5-carboxylic acid (XXIII).—5-Cyano-3-methylisothiazole (5·0 g.) was boiled with 2N-sodium hydroxide (50 c.c.) until dissolution was complete. The cooled, filtered solution was acidified with concentrated hydrochloric acid, to give the *acid* (5·35 g.), colourless needles, m. p. 206° (decomp.) (from water) (Found: C, 41·8; H, 3·8; N, 9·45; S, 22·5. $C_5H_5O_2NS$ requires C, 41·8; H, 3·5; N, 9·8; S, 22·4%).

3-Methylisothiazole (XXVI).—3-Methylisothiazole-5-carboxylic acid (6·3 g.) was gently heated over a free flame. *3-Methylisothiazole* (3·0 g.) distilled at 125—135°/751 mm. Redistillation gave a colourless, mobile liquid, b. p. 133°/751 mm., (n_D^{21} 1·5180) (Found: C, 48·6; H, 5·0; N, 13·9; S, 32·1. C_4H_5NS requires C, 48·45; H, 5·1; N, 14·1; S, 32·3%), having an odour similar to that of isothiazole.

3-Methyl-5-thiocarbamoylisothiazole.—5-Cyano-3-methylisothiazole (24·0 g.) in pyridine (240 c.c.) was saturated with hydrogen sulphide during 8 hr. Removal of the solvent gave *3-methyl-5-thiocarbamoylisothiazole* (26·0 g.; m. p. 160—162°) which recrystallized from benzene in yellow needles, m. p. 163—164° (Found: C, 38·25; H, 4·0; N, 17·6. $C_5H_6N_2S_2$ requires C, 37·95; H, 3·8; N, 17·7%).

Methyl 3-Methylisothiazole-5-carboxylate.—Powdered 3-methylisothiazole-5-carboxylic acid (22·0 g.) was added to ethereal (600 c.c.) diazomethane, prepared from *N*-nitrosomethylurea (60 g.). After 16 hr., evaporation gave the *ester* (21·5 g.). Distillation gave colourless needles, m. p. 29°, b. p. 100°/11 mm. (Found: C, 45·8; H, 4·5; N, 8·7; S, 20·4. $C_6H_7O_2NS$ requires C, 45·8; H, 4·5; N, 8·9; S, 20·4%).

3-Methylisothiazole-5-carboxyhydrazide.—The methyl ester (21·5 g.) and 100% hydrazine hydrate (21·5 c.c.) dissolved in alcohol (80 c.c.) were heated at 100° for 30 min. After 3 hr.,

XUM

filtration gave the *hydrazide* (19·3 g.) which recrystallized from water in cream plates, m. p. 167—168° (Found: C, 38·5; H, 4·5; N, 26·75. $C_5H_7ON_3S$ requires C, 38·2; H, 4·5; N, 26·7%).

3-*Methyl*-4-*nitroisothiazole* (XXX).—Potassium nitrate (6·0 g.) was slowly stirred into a solution of 3-methylisothiazole (6·0 g.) in 20% oleum (15 c.c.) at 20—30°, and the mixture was set aside at room temperature for 16 hr. before being heated at 100° for 24 hr. The cold solution was added to ice (150 g.), neutralized with sodium carbonate, and extracted with ether (3 × 100 c.c.). Evaporation of the dried ($MgSO_4$) extracts gave 3-*methyl*-4-*nitroisothiazole* (7·1 g.) which distilled as a yellow oil (6·2 g.), b. p. 108°/14 mm. (Found: C, 33·65; H, 3·05; N, 19·1. $C_4H_4O_2N_2S$ requires C, 33·3; H, 2·8; N, 19·4%).

4-*Amino*-3-*methylisothiazole* (XXXI).—Aqueous ammonia (*d* 0·88; 70 c.c.) and 3-methyl-4-nitroisothiazole (4·0 g.) in hot alcohol (150 c.c.) were divided into 3 equal portions which were added at 5 min. intervals to a boiling, vigorously stirred solution of ferrous sulphate ($7H_2O$; 61 g.) in water (195 c.c.). Boiling was continued for 15 min., inorganic material was removed, and the filtrate and alcoholic washings were evaporated to dryness. Concentration of dried ($MgSO_4$) ethereal extracts (2 × 250 c.c.) of the residue gave crude 4-*amino*-3-*methylisothiazole* (2·1 g.). Distillation yielded colourless prisms (1·7 g.), b. p. 63°/0·08 mm., m. p. 28° (Found: C, 42·0; H, 5·3; N, 24·2. $C_4H_6N_2S$ requires C, 42·1; H, 5·3; N, 24·5%). The hydrated acetyl derivative separated from water in needles, m. p. 62—63°, unstable to drying. A satisfactory analysis could not be obtained (Found: C, 35·3; H, 7·3; N, 12·6; S, 15·5; H_2O, 26·4. Calc. for $C_6H_8ON_2S,3H_2O$: C, 34·3; H, 6·7; N, 13·3; S, 15·25; H_2O, 25·7%).

4-p-*Acetamidobenzenesulphonamido*-3-*methylisothiazole*.—*p*-Acetamidobenzenesulphonyl chloride (2·33 g.) was added at <10° to 4-amino-3-methylisothiazole (1·14 g.) in pyridine (10 c.c.), and the solution set aside for 16 hr. Treatment with ice (200 g.) and 2N-hydrochloric acid (100 c.c.) gave 4-p-*acetamidobenzenesulphonamido*-3-*methylisothiazole* (2·7 g.), m. p. 192—196°. Repeated dissolution in 0·5N-ammonia (charcoal) and reprecipitation with N-acetic acid gave a white powder, m. p. 198—199° (Found: C, 46·15; H, 4·3; N, 13·2. $C_{12}H_{13}O_3N_3S_2$ requires C, 46·3; H, 4·2; N, 13·5%).

4-p-*Aminobenzenesulphonamido*-3-*methylisothiazole* (XXXII).—4-*p*-Acetamidobenzenesulphonamido-3-methylisothiazole (2·7 g.) was boiled for 2 hr. with 2N-sodium hydroxide (25 c.c.) (charcoal), and the cooled, filtered solution acidified with acetic acid. The *aminobenzenesulphonamide* (2·15 g.) separated from alcohol in colourless prisms, m. p. 175° (Found: C, 44·25; H, 4·3; N, 15·8; S, 23·8. $C_{10}H_{11}O_2N_3S_2$ requires C, 44·6; H, 4·1; N, 15·6; S, 23·8%).

The authors thank the Directors of May and Baker, Ltd. for permission to publish this work, Professor C. A. Coulson and the staff of the Summer School of Theoretical Chemistry, Oxford for advice on the electron-density calculations, Mr. S. Bance, B.Sc., A.R.I.C., for the microanalyses, Messrs. J. S. Goddard and R. L. G. Keith for technical assistance, and many of their other colleagues for helpful discussion.

Research Laboratories, May & Baker, Ltd.,
Dagenham, Essex.

[*Received, January 23rd,* 1959.]

614. *Alkali-metal Derivatives of Sucrose. Part III.*[1] *The Composition of the Mono-O-methylsucrose prepared from a Trisodium Derivative.*

By W. A. P. Black, E. T. Dewar, and D. Rutherford.

A trisodium derivative of sucrose with methyl toluene-*p*-sulphonate gives a mixture of sucrose and its methyl ethers. A mono-*O*-methylsucrose isolated from this is a mixture of isomers, mainly those containing the substituent methyl group at position 2 of the glucose unit or position 1 of the fructose unit. Substitution also occurs at positions 3 and 6 of the fructose and the glucose moiety respectively, and is not restricted to these positions. The significance of these results on the location of the sodium atoms in the original derivative is discussed.

The preparation of sodium derivatives of sucrose, by reaction of sodium or sodium amide with sucrose in liquid ammonia at −33°, and their condensation with organic chloro-compounds, have been previously described.[1,2] This paper describes the structures of mono-*O*-methylsucroses prepared from a trisodium derivative.

The white crystalline monosodium derivative contains 4·47% of ammonia [2] and can be considered as a true alkoxide containing one mol. of ammonia ($C_{12}H_{21}O_{11}Na,NH_3$) or as a sodamide addition compound ($C_{12}H_{22}O_{11},NaNH_2$). This could not be methylated with methyl iodide because the ammonia was methylated preferentially, with the formation of hydriodic acid which decomposed the sodium derivative. The more highly substituted derivatives, however, contain less ammonia (1·4—2·7%),[2] and methylation can be achieved although the reaction is not quantitative, again owing to the presence of ammonia. The trisodium compound used in this investigation (NH_3, 2·13%) gave a product with MeO = 10·6%, whereas quantitative methylation of the trisodium alkoxide, $C_{12}H_{19}O_{11}Na_3$, should give tri-*O*-methylsucrose (MeO = 24·2%).

Of many liquids tried as methylating media, the most successful was tri-*O*-methylglycerol.[3,4] Methyl toluene-*p*-sulphonate was found to be a satisfactory methylating agent for the trisodium derivative at the level of 1 mol. per sodium atom, so that no excess of reagent was present. Except for cellulose,[5] toluene-*p*-sulphonic esters have not often been used for alkylation of carbohydrates. The sodium derivative in tri-*O*-methylglycerol was heated with methyl toluene-*p*-sulphonate at 110° for 5 hr. with vigorous stirring, the mixture was dissolved in water, and the solution de-ionised and concentrated to give a glassy methylated material (OMe, 10·6%). Chromatography revealed it as a mixture of sucrose, mono- and di-*O*-methylsucrose, and more highly methylated material. The components were partly separated on a cellulose column,[6] the following fractions (total 86%) being obtained. Fraction 1 (16·3%) contained only sucrose. Fraction 2 (24·9%) was sucrose containing a small amount of mono-*O*-methylsucrose. Fraction 3 (20·0%) was chiefly mono-*O*-methylsucrose containing some di-*O*-methylsucrose. Fraction 4 (21·8%) was di-*O*-methylsucrose and more highly methylated products.

Refractionation of fraction 3 on cellulose and further purification gave a pale yellow glass, $[\alpha]_D$ +60·6° in water, which gave correct analyses for a mono-*O*-methylsucrose (OMe, 8·3%). Chromatography in two solvent systems indicated that this was homogeneous. Periodate oxidation in the dark at 20° followed closely that of sucrose, 2·7 mols. of periodate being consumed and 0·86 mol. of formic acid produced after 24 hr. This suggests that there was little substitution on secondary hydroxyl groups, a result which was not confirmed by hydrolysis. Indeed, with 0·05N-sulphuric acid it gave a mixture

[1] Part II, Black, Dewar, Paterson, and Rutherford, *J. Appl. Chem.*, 1959, **9**, 256.
[2] Arni, Black, Dewar, Paterson, and Rutherford, *J. Appl. Chem.*, 1959, **9**, 186.
[3] Dr. D. J. Bell, personal communication.
[4] Fairbourne, Gibson, and Stephens, *Chem. and Ind.*, 1930, **49**, 1021.
[5] Weaver, MacKenzie, and Shirley, *Ind. Eng. Chem.*, 1954, **46**, 1490.
[6] Hough, Jones, and Wadman, *J.*, 1949, 2511.

of sugars which was separated on a cellulose column [6] into a mono-*O*-methylhexose fraction (9·3 parts), D-fructose (4·0 parts), and D-glucose (7·4 parts). This ether fraction was separated on thick paper into 2- (2·4 parts) and 6-*O*-methyl-D-glucose (1·0 part) and 1- (2·1 parts) and 3-*O*-methyl-D-fructose (1·5 parts), and two other unidentified ethers which were present in smaller amounts. 2- and 6-*O*-Methyl-D-glucose and 1-*O*-methyl-D-fructose were characterised by their methoxyl contents, optical rotations, chromatography with authentic samples, periodate oxidation, and osazone formation. The second mono-*O*-methylfructose component (OMe, 15·8%) was obtained crystalline and had $[\alpha]_D$ −54·8° in water, which strongly suggested that it was 3-*O*-methyl-D-fructose ($[\alpha]_D$ −53·5° in water [7]); 4-*O*-methyl-D-fructose ($[\alpha]_D$ −87·5° in water) has not been obtained crystalline [8] and 6-*O*-methyl-D-fructofuranose has a positive rotation.[9] However, the structure of this component could not be confirmed by periodate oxidation or osazone formation, owing probably to loss of water and formation of difructose anhydride during extensive drying.[10]

The presence of glucose, fructose, and at least two glucose and two fructose monomethyl ethers proves that the " chromatographically pure " mono-*O*-methylsucrose is a mixture of isomers, and this was confirmed by extensive development of the unhydrolysed material in a third solvent, by which two spots and a trace of another were identified. Because of the small quantities available and the difficulties of separating quantitatively a mixture containing six mono-*O*-methylhexoses, the proportions of the components of the hydrolysate must be considered only approximate. Nevertheless, some observations can be made. For example, from the relative proportions of unsubstituted glucose and fructose present, which are easily separated quantitatively, substitution occurs to a greater extent on the fructose than on the glucose moiety. From the distribution of mono-*O*-methylhexoses, substitution occurs chiefly at position 2 and to a smaller extent at position 6 of the glucose residue, and in the fructose residue $C_{(1)}$ is the most active centre closely followed by $C_{(3)}$. These results agree with previous views on the relative reactivities of hydroxyl groups in the glucose molecule in alkaline media.[11] The ratio of the rate constants for the methylation of alkali cellulose with methyl chloride was shown to be 5 : 1 : 2 for positions 2, 3, and 6 of the glucose residue,[12] and 4·5 : 1 : 2 for ethylation with ethyl chloride.[13] Percival,[14] however, found that methylation of a sucrose–tripotassium hydroxide compound gave a tri-*O*-methylsucrose substituted at the three primary alcohol groups, indicating that the potassium hydroxide was associated with the primary alcohol groups in the original addition compound.

It must be borne in mind, however, in the present study that the methoxyl content of the material was less than half that calculated from the quantitative replacement of sodium atoms. Further, the composition of the other methyl ethers formed has not yet been determined. Consequently, the location of much of the sodium present in the original trisodium derivative is still unknown, but sufficient has been done to indicate that analysis of the methylated products from sodium derivatives will be extremely complex.

Experimental

Analytical Methods.—Solutions were evaporated under reduced pressure below 60°. Paper-partition chromatography was on Whatman No. 1 paper at 20° with the following solvent systems (v/v): (1) butan-1-ol–ethanol–water (40 : 11 : 19); (2) (ethyl methyl ketone half saturated with water)–ammonia (99 : 1); (3) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3).

[7] Anderson, Charlton, Haworth, and Nicholson, *J.*, 1929, 1337.
[8] Barry and Honeyman, *Adv. Carbohydrate Chem.*, 1952, **7**, 81.
[9] MacDonald and Jackson, *J. Res. Nat. Bur. Stand.*, 1940, **24**, 181.
[10] MacDonald, *Adv. Carbohydrate Chem.*, 1946, **2**, 265.
[11] Sugihara, *ibid.*, 1953, **8**, 1.
[12] Croon and Lindberg, *Svensk Papperstidn.*, 1957, **60**, 843.
[13] Croon and Flamm, *ibid.*, 1958, **61**, 963.
[14] Percival, *J.*, 1935, 648.

Papers were sprayed with α-naphthol–phosphoric acid,[15] benzidine–trichloroacetic acid,[16] 3% *p*-anisidine hydrochloride in butan-1-ol,[17] and aniline hydrogen oxalate and phthalate.[18] R_{Glu}, R_{Suc}, R_{Fru}, and R_F are the rates of travel relative to glucose, sucrose, fructose, and the solvent front respectively. Electroionophoresis [19] was carried out in borate buffer of pH 10. Whatman 3MM sheets, after preliminary extraction with hot benzene–ethanol (1 : 1), were used for the chromatographic separation of the mono-*O*-methylhexose fraction. Unless otherwise stated, specific rotations were measured in water at 20°.

Materials.—The trisodium derivative was prepared as described in Part I [2] and gave the following analysis: sodium, 16·4; sucrose (as $C_{12}H_{22}O_{11}$), 81·3; ammonia, 2·13%; sodium atoms per sucrose mol., 3·00. Commercial (Eastman Organic Chemicals) methyl toluene-*p*-sulphonate was purified before use by dissolution in chloroform, drying (Na_2SO_4), recovery, and distillation, the fraction boiling at 132°/1—2 mm. being used. Tri-*O*-methylglycerol was prepared by exhaustive methylation of epichlorohydrin.[4]

Methylation of the Trisodium Derivative.—The compound (6·082 g.) was dispersed in tri-*O*-methylglycerol (30 ml.), methyl toluene-*p*-sulphonate (1 mol. per Na atom) added, and the mixture heated at 110° for 5 hr. with stirring and exclusion of moisture. The mixture was dissolved in water (50 ml.), and the solution de-ionised (Amberlite resins IR-120-H^+ and IR-45-OH^-) and evaporated to a glass (4·962 g.) (Found: OMe, 10·6%). In a second experiment, the derivative (4·223 g.) gave a glass (3·371 g.; OMe, 10·5%).

Fractionation of the Glass.—The combined products (8·33 g.) were fractionated on a cellulose column [6] (50 × 3·8 cm.) with butan-1-ol saturated with water as eluant, partial separation being effected:

Fraction 1 (1·356 g.), R_F identical with that of sucrose. The material was purified by treatment with charcoal, and the syrup crystallised from methanol {m. p. 178°; $[\alpha]_D$ +66·4° (*c* 2); Found: C, 41·9; H, 6·5. $C_{12}H_{22}O_{11}$ requires C, 42·1; H, 6·5%}. Identity was confirmed by conversion with sodium acetate–acetic anhydride [20] into sucrose octa-acetate, m. p. 86—88° (Found: C, 49·2; H, 5·7. Calc. for $C_{28}H_{38}O_{19}$: C, 49·6; H, 5·6%).

Fraction 2 (2·074 g), sucrose containing a small amount of mono-*O*-methylsucrose.

Fraction 3 (1·661 g.), mono-*O*-methylsucrose and some di-*O*-methylsucrose.

Fraction 4 (1·819 g.), di-*O*-methylsucrose and higher methylated material.

The identification of the components of fractions 2—4 was based on the relative positions of the spots on paper chromatography (solvent 1), with di-*O*-methylsucrose and 1′,4,6′-tri-*O*-methylsucrose [21] as reference spots. Both α-naphthol–phosphoric acid [15] and *p*-anisidine hydrochloride [17] are extremely sensitive sprays for detecting sucrose methyl ethers.

Isolation of Mono-O-methylsucrose from Fraction 3.—Fraction 3 (1·66 g.) was refractionated on a tightly packed cellulose column [6] with butan-1-ol saturated with water as the eluant, to give a mono-*O*-methyl (812 mg.) and a di-*O*-methyl fraction (241 mg.). After further purification, the mono-*O*-methylsucrose (629 mg.) was obtained as a pale yellow, non-reducing glass, $[\alpha]_D$ +60·6° (*c* 2·1) (Found: OMe, 8·3. $C_{13}H_{24}O_{11}$ requires OMe, 8·7%). Paper chromatography (solvent 1) over an extended period showed a single spot (R_{Glu} 1·11, R_{Suc} 1·44); solvent 2 also revealed only one spot. After the hydrolysis had proved that the material was a mixture of isomers, chromatography was repeated with solvent 3, two spots (R_{Glu} 1·01, 1·15) and a trace of another (R_{Glu} 1·27) being detected.

Periodate Oxidation of Mono-O-methylsucrose.—A 0·1% solution (10 ml.) was treated with 0·025M-sodium periodate (10 ml.) in the dark at 20°, and aliquot parts (2 ml.) were removed for estimation of periodate uptake [22] and formic acid liberated.[23] The ether consumed 1·99 (1 hr.), 2·26 (3 hr.), 2·41 (6 hr.), 2·71 (24 hr.), 2·82 (48 hr.) mols. of periodate and liberated 0·38, 0·62, 0·70, 0·86, 0·81 mol. of formic acid. Under identical conditions, sucrose consumed 1·76, 2·51, 2·59, 2·96, 3·01 mols. of periodate and liberated 0·19, 0·29, 0·40, 0·63, 0·65 mol. of formic acid.

Separation of the Sugars obtained on Hydrolysis of Mono-O-methylsucrose.—The glass (352 mg.)

[15] Albon and Gross, *Analyst*, 1952, **77**, 410.
[16] Whelan, Bailey, and Roberts, *J.*, 1953, 1297.
[17] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[18] Partridge, *Nature*, 1949, **164**, 443.
[19] Foster, *Chem. and Ind.*, 1952, 1050.
[20] French, *J. Amer. Chem. Soc.*, 1955, **77**, 1024.
[21] McKeown, Serenius, and Hayward, *Canad. J. Chem.*, 1957, **35**, 28.
[22] Jackson, "Organic Reactions," Chapman and Hall Ltd., London, 1944, Vol. II, p. 361.
[23] Halsall, Hirst, and Jones, *J.*, 1947, 1399.

XUM

was heated with 0·05N-sulphuric acid (10 ml.) at 100° for 3 hr. ($[\alpha]_D$ −6·5°). The cooled solution was neutralised (Phenol Red) with 0·1N-sodium hydroxide, ethanol (150 ml.) added to precipitate sodium sulphate, and the centrifugate concentrated to a syrup, which was fractionated on a cellulose column [6] with butan-1-ol saturated with water as the eluant:

Fraction A (135 mg.) was a mixture of mono-*O*-methylhexoses which were separated on thick paper as described below.

Fraction B (58 mg.) was D-fructose. The syrup was shaken for 5 hr. with anhydrous acetone (5 ml.) containing a trace of sulphuric acid, and then treated as described by Bell [21] to give 1,2:4,5-di-*O*-isopropylidene-D-fructose (34 mg.) as needles, m. p. and mixed m. p. 117—118°, $[\alpha]_D$ −143° (*c* 1 in chloroform). Under the same conditions, 23·4 mg. of 1,2:4,5-di-*O*-isopropylidene-D-fructose were obtained from 40 mg. of authentic D-fructose.

Fraction C (107 mg.) was D-glucose, which was heated with sodium acetate (50 mg.) and acetic anhydride (1 ml.) at 100° for 2 hr. to give penta-*O*-acetyl-β-D-glucose (115 mg.). Recrystallisation from absolute ethanol gave needles, m. p. and mixed m. p. 128°, $[\alpha]_D$ +4·5° (*c* 4·9 in chloroform).

Fraction A (122 mg.) was separated on thick paper with solvent 2:

Fraction A1 (13·1 mg.), R_{Glu} 4·03 (solvent 2), identical with authentic 6-*O*-methyl-D-glucose, $[\alpha]_D$ +53° (*c* 0·5) (Found: OMe, 14·9%. Calc. for $C_7H_{14}O_6$: OMe, 16·0%). The sugar consumed 2·5 (3 hr.), 2·4 (24 hr.), 2·5 (48 hr.) mols. of periodate and liberated 0·15, 0·15, 0·14 mol. of formaldehyde, the latter being estimated by the micro-colorimetric method of Hough, Powell, and Woods,[25] with D-mannitol as a source of formaldehyde for the calibration graph. 6-*O*-Methyl-D-glucose would be expected to give negligible amounts of formaldehyde. The structure was confirmed by the partial periodate oxidation method of Lemieux and Bauer.[26] Fraction A1 and authentic 6-*O*-methyl-D-glucose gave identical yellow spots, R_F 0·78 (solvent 1), with fainter spots, R_F 0·60, when chromatograms were sprayed with 1% aniline hydrogen phthalate in water-saturated butan-1-ol. On treatment with 10% (v/v) acetic acid (0·5 ml.) and freshly distilled phenylhydrazine (0·04 ml.) at 80° for 3 hr.,[27] fraction A1 (9·4 mg.) gave 6-*O*-methyl-D-glucose phenylosazone (2·9 mg.), m. p. and mixed m. p. 184° (Found: OMe, 7·7. Calc. for $C_{19}H_{24}O_4N_4$: OMe, 8·3%).

Fraction A2 (31·8 mg.), R_{Glu} 5·00 (solvent 2) (authentic 2-*O*-methyl-D-glucose gave R_{Glu} 4·83), $[\alpha]_D$ +58° (*c* 1·5) (Found: OMe, 15·5%). The sugar crystallised but the quantity was insufficient to afford an accurate m. p. It consumed 3·8 (3 hr.), 3·9 (24 hr.), 4·5 (48 hr.) mols. of periodate and liberated 0·10, 0·28, 0·36 mol. of formaldehyde. Authentic 2-*O*-methyl-D-glucose consumed 4·4 (3 hr.), 4·5 (24 hr.), 4·8 (48 hr.) mols. of periodate and liberated 0·17, 0·43, 0·58 mol. of formaldehyde. Partial periodate oxidation at 0° for 1 hr.[26] gave a strong lemon-yellow spot in the cold (R_F 0·28, solvent 1) for both fraction A2 and authentic 2-*O*-methyl-D-glucose. It gave a negative formazan test with triphenyltetrazolium hydroxide,[28] indicating that position 2 was substituted. Fraction A2 (24·8 mg.), on treatment with phenylhydrazine as before,[27] gave D-glucose phenylosazone (8·6 mg.), m. p. and mixed m. p. 205°, with a negligible methoxyl content.

Fraction A3 (27·7 mg.), R_{Fru} 3·62 (solvent 2), identical with authentic 1-*O*-methyl-D-fructose, $[\alpha]_D$ +64·5 (*c* 1·1) (Found: OMe, 15·1. Calc. for $C_7H_{14}O_6$: OMe, 16·0%). The sugar consumed 3·1 (3 hr.), 3·2 (24 hr.), 3·2 (48 hr.), 3·4 (72 hr.) mols. of periodate and liberated 0·18, 0·33, 0·52, 0·49 mol. of formaldehyde. Authentic 1-*O*-methyl-D-fructose consumed 3·5, 3·7, 3·6, 3·5 mols. of periodate and liberated 0·28, 0·74, 0·75, 0·74 mol. of formaldehyde. The above, slightly low results for the specific rotation, methoxyl content, periodate consumption, and formaldehyde production compared with those for the authentic, crystalline sugar can be attributed to the extreme difficulty in drying syrupy fructose methyl ethers.

Fraction A3 (12·1 mg.) was treated with phenylhydrazine [27] to give D-glucose phenylosazone (4·4 mg.), m. p. and mixed m. p. 207—208°, with a negligible methoxyl content.

Fraction A4 (19·2 mg.), R_{Fru} 4·02 (solvent 2), identical with authentic 3-*O*-methyl-D-fructose, $[\alpha]_D$ −54·8° (*c* 1·82) (Found: OMe, 15·8%). The sugar crystallised but the quantity available was insufficient to afford an accurate m. p. 4-*O*-Methyl-D-fructose ($[\alpha]_D$ −87·5°) has not been obtained crystalline.[8] After extensive drying over phosphoric oxide (60°/0·5 mm.), fraction A4

[24] Bell, *J.*, 1947, 1461.
[25] Hough, Powell, and Woods, *J.*, 1956, 4799.
[26] Lemieux and Bauer, *Canad. J. Chem.*, 1953, **31**, 814.
[27] Smith, *J.*, 1951, 2646.
[28] Wallenfels, *Naturwiss.*, 1950, **37**, 491.

consumed 0·8 (48 hr.), 0·8 (72 hr.) mol. of periodate and liberated 0·30, 0·37 mol. of formaldehyde. 3-*O*-Methyl-D-fructose consumed 3·4, 3·5 mols. of periodate and liberated 0·98, 1·13 mol. of formaldehyde; for 4-*O*-methyl-D-fructose the results were 1·8, 2·7, and 1·16, 1·18 respectively. It is suggested that the anomalous results for fraction A4 are due to anhydride formation [10] during drying. Attempts to form an osazone were also unsuccessful. Electroionophoresis gave no appreciable mobility.

This work forms part of Project No. 132 of the Sugar Research Foundation, Inc., and the authors are indebted to Dr. H. B. Hass for permission to publish it. Thanks are expressed to Dr. E. E. Percival for advice and carrying out the electrophoresis experiments and to Dr. D. J. Bell, Dr. S. Bayne, Dr. L. D. Hayward, and Dr. B. Lindberg for gifts of samples.

ARTHUR D. LITTLE RESEARCH INSTITUTE, INVERESK, MUSSELBURGH, MIDLOTHIAN. [*Received, March 2nd*, 1959.]

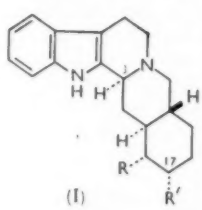
---

615. *The Rotatory Dispersion of Yohimbine and Some Derivatives.*

By J. A. D. JEFFREYS.

The rotatory dispersion for visible light of yohimbine, yohimbone, yohimbane, ψ-yohimbine, and ψ-yohimbane in water (as salts), in methanol, and in chloroform are analysed in terms of the equation $[M] = A/(\lambda^2 - 0{\cdot}08) + B/\lambda^2$ (λ in mμ × 10^{-3}), and the results discussed.

THE rotatory dispersions of yohimbone and of yohimbane in dioxan have been described; [1] for the former the dispersion is dominated by a large component due to the carbonyl group, while in the case of yohimbane the indole band with $\lambda_{max.}$ at about 280 mμ is only weakly active. As the stereochemistry of yohimbine and its derivatives is known, and because changes in the numerators of the Drude terms describing the dispersions might be more informative than molecular-rotation differences measured at a single wavelength, the optical rotations for visible light of yohimbine (I; R = CO_2Me, R′ = OH), yohimbone (I; R = H, C:O at position 17), yohimbane (I; R = R′ = H), and their epimers at position 3 were chosen for examination. However, after attempts to prepare ψ-yohimbane by two routes had failed to give useful yields, preparation of this compound was abandoned.



(I)

EXPERIMENTAL

Materials.—The starting material was yohimbine hydrochloride; before use, the free base was recrystallised from ethyl acetate, then from ether. The sample used for the dispersion measurements had m. p. 234—236° (decomp.) (lit.,[2] 234°), and the specific rotation as the sulphate in water had values (given below) that could be expressed by the equation $[\alpha]_D^{16} = 114{\cdot}5c^{0{\cdot}085}$ (c = concentration of base in g. per 100 ml. of solution):

Concentration	1·617	1·043	0·8086	0·6469	0·4043
α found, 2 dm. tube	3·86°	2·39° [a]	1·82°	1·44°	0·86°
α calculated	3·86°	2·40°	1·82°	1·43°	0·86°

[a] At 22°; value taken from Table 1.

This equation predicts a value for the specific rotation of yohimbine hydrochloride which is higher than that found by Janot and Goutarel [3] (found, $[\alpha]_D$ +96·9°, *c* 1; calc., +103·8°), but ones that agree with the figures quoted by Hahn and Brandenberg [4] ($[\alpha]_D^{20}$ +103—104°, *c* 1; calc., +103·8°) and by Warnat [5] (found, $[\alpha]_D^{25}$ +101·9°, *c* 0·800; calc., +101·0°).

[1] Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362.
[2] Witkop, *Annalen*, 1943, **554**, 83.
[3] Janot and Goutarel, *Bull. Soc. chim. France*, 1949, **16**, 509.
[4] Deutsches Artzneibuch, quoted by Hahn and Brandenberg, *Ber.*, 1927, **60**, 707.
[5] Warnat, *Ber.*, 1930, **63**, 2959.

XUM

Yohimbone was prepared by Oppenauer oxidation of yohimbic acid.[2] The rigorous drying of the reagents specified was unnecessary, as water was evolved during the reaction. The product had m. p. 288° (decomp.), $[\alpha]_D^{19}$ −109° (*c* 0·759 in pyridine) {lit., m. p. 307° (decomp.), $[\alpha]_D$ −106° (*c* 0·65 in pyridine)}.

Yohimbane was prepared by Wolff–Kischner reduction of yohimbone by the method used for the conversion of *ψ*-yohimbone into yohimbane.[6] The product, which showed no carbonyl absorption in the infrared spectrum, had m. p. 204° (decomp.), $[\alpha]_D^{21}$ −115° (*c* 0·496 in pyridine) {lit., m. p. 205—206°, $[\alpha]_D$ −115° (*c* 1 in pyridine)}.

ψ-Yohimbine was prepared in 10—20% yield by dehydrogenation of yohimbine, then reduction,[7] and was easily separated from the other products of the reaction by recrystallisation from methanol, in which it is sparingly soluble; recycling the crude recovered yohimbine raised the overall yield to about 30%. The product had m. p. 264° (decomp., effervescence), $[\alpha]_D^{23}$ +29° (*c* 0·9095 in pyridine) {lit., m. p. 268°; [6] 277—278°; [7] $[\alpha]_D^{19}$ +28° (*c* 1 in pyridine) [7]}.

ψ-Yohimbone was prepared from *ψ*-yohimbine by the method described by Witkop.[2] The product had m. p. 268—270° (decomp.) (lit., m. p. 268°), and $[\alpha]_D^{22}$ −17° (*c* 0·94 in pyridine). A previous determination, on different samples of *ψ*-yohimbone and pyridine, gave $[\alpha]_D^{18}$ −17° (*c* 0·621). These figures do not agree with the value in the literature [6] of $[\alpha]_D^{20}$ −24° (*c* 1 in pyridine).

With the exception of yohimbane, the final recrystallisation of each base was from ether; the use of a higher-boiling solvent was accompanied by some oxidation of the base. Yohimbane was precipitated by methanol from a concentrated solution in ether, and the product dried at 100°/16 mm. for not less than 2 hr.

Attempted Preparation of ψ-Yohimbane.—(*a*) (cf. ref. 8). Hydrogen chloride was passed through a solution of *ψ*-yohimbone (100 mg.) in glacial acetic acid (10 ml.) and ethanedithiol (1 ml.) for 30 min.; after being kept overnight at room temperature, the solution was evaporated to dryness on a steam-bath under reduced pressure. Recrystallisation of the residue from benzene–light petroleum (b. p. 100—120°) gave the *ethylene dithioacetal* of *ψ*-yohimbone as aggregates, m. p. 218—222° (decomp.) (Found: C, 68·0; H, 6·95. $C_{21}H_{26}N_2S_2$ requires C, 68·1; H, 7·0%). Treatment of this with Raney nickel in boiling ethanol caused extensive decomposition, but a trace of an unidentified crystalline substance, m. p. 262°, was isolated.

(*b*) (cf. ref. 9) Yohimbane was dehydrogenated by mercuric acetate, and the product reduced with zinc and glacial acetic acid. The chief crystalline product was yohimbane, but repeated recrystallisation from methanol gave a small yield of *ψ*-yohimbane, m. p. 99° (lit., 96—97°). Its hydrochloride and sulphate were both insoluble in cold water.

Solvents.—(*a*) The base was suspended in distilled water, a small excess (0·00—0·02 ml.) over the calculated volume of N-acid added, and the solution made up to 20 ml.

(*b*) " AnalaR " methanol was used without further purification; it had $n_D^{17\cdot2}$ 1·3297; pure methanol has $n_D^{17\cdot2}$ 1·3297 (by interpolation).[10a]

(*c*) " AnalaR " chloroform was washed once with an equal volume of 2N-sodium carbonate, five times with an equal volume of distilled water, dried (Na_2SO_4), and distilled through an 18" column packed with nickel wire. The sample used had b. p. 61·5°/760 mm., n_D^{18} 1·4471. Pure chloroform has b. p. 61·3°/760 mm., n_D^{18} 1·4468.[10b] Carbon tetrachloride is the most probable impurity, and the refractive index suggests the presence of *ca.* 2%; the impurity was not ethanol, as this lowers both the b. p.[11a] and the refractive index [11b] of chloroform. The point is important, as the optical activity of yohimbine in solution in chloroform is markedly affected by traces of ethanol:

Ethanol (%) in chloroform	0	*ca.* 1 [a]	2
$[\alpha]_D$/Temperature	+3°/21°	+9°/17°	+10°/21°

[a] Commercial chloroform.

[6] Janot, Goutarel, Le Hir, Amin, and Prelog, *Bull. Soc. chim. France*, 1952, **19**, 1085.
[7] Weisenborn and Diassi, *J. Amer. Chem. Soc.*, 1956, **78**, 2022.
[8] Huebner, St. Andre, Schlittler, and Uffer, *ibid.*, 1955, **77**, 5725.
[9] Wenkert and Roychaudhuri, *ibid.*, 1956, **78**, 6417.
[10] Timmermans, " Physico-Chemical Constants of Pure Organic Compounds," Elsevier Publ. Co., New York, 1950, (*a*) p. 305, (*b*) p. 220.
[11] International Critical Tables, MacGraw-Hill Book Co. Inc., New York, 1933, (*a*) Vol. III, p. 312, (*b*) Vol. VII, p. 78.

Because of the low solubilities of some of the compounds, all the solutions were dilute, to avoid an excessive scatter in the range of concentrations; necessarily, the angles of rotation were small.

Apparatus.—A Hilger Microptic polarimeter was used with the same 2 dm. tube and end-plates throughout; the tube was sealed against leakage by coating the ground faces with high-vacuum grease for aqueous and methanolic solutions, and with glycerol for solutions in chloroform. With chloroform this sealing was important; if the seal was defective the solution darkened, and after an induction period the values of α drifted, even though there was no apparent leakage of the solution. Runs in which this occurred were discarded.

A Leitz sodium lamp, an Osram cadmium lamp, and a K.B.B. mercury-in-quartz arc were used. Readings for lines other than the D-line were made by using a set of Perkin eyepieces (slitless direct-vision spectroscopes); to read the rotation for Hg 4047 Å. a filter was used as well. The rotations quoted in Table 1 are the means of at least 10 readings; those for Hg 4047 Å. are less precise than for other lines.

TABLE 1. *Observed and calculated optical rotations.*

Yohimbine	Water [a] *c* 1·0430; 22°. α		Methanol *c* 1·3125; 22°. α		Chloroform *c* 1·3045; 21°. α	
Wavelength (Å)	Found	Calc.	Found	Calc.	Found	Calc.
6438	+1·95°	+1·95°	+1·41°	+1·36°	+0·05°	+0·05°
5893	2·39	2·39	1·66	1·66	0·08	0·08
5780 [b]	2·50	2·50	1·74	1·75	0·10	0·09
5461	2·87	2·86	1·99	1·99	0·12	0·12
5086	3·41	3·41	2·39	2·38	0·17	0·17
4800	3·96	3·95	2·73	2·76	0·22	0·24
4358	5·13	5·13	3·62	3·62	0·43	0·42
Yohimbone	*c* 0·3830; 21°.		*c* 0·1558; 21°.		*c* 0·7380; 19°.	
6438	−0·22	−0·22	−0·20	−0·19	−1·16	−1·12
5893	0·25	0·26	0·23	0·23	1·40	1·40
5780 [b]	0·27	0·27	0·24	0·24	— [c]	—
5461	0·31	0·31	0·28	0·28	1·69	1·70
5086	0·37	0·36	0·33	0·33	2·07	2·07
4800	0·40	0·41	0·38	0·38	2·45	2·45
4358	0·52	0·52	0·48	0·48	3·30	3·31
Yohimbane [d]			*c* 0·2465; 20°.		*c*, 0·2385; 20°.	
6438	—	—	−0·32	−0·32	−0·34	−0·32
5893	—	—	0·38	0·38	0·38	0·38
5780 [b]	—	—	0·40	0·39	0·40	0·40
5461	—	—	0·44	0·44	0·45	0·45
5086	—	—	0·51	0·50	0·52	0·52
4800	—	—	0·56	0·56	0·59	0·59
4358	—	—	0·66	0·67	0·70	0·72
4047	—	—	0·80	0·76	0·89	0·85
ψ-Yohimbine [e]	*c* 0·8350; 20°.		*c* 0·5115; 22°.		*c* 0·7420; 23°.	
6438	−0·15	−0·11	−0·12	−0·11	−0·56	−0·52
5893	0·18	0·18	0·15	0·16	0·68	0·70
5780 [b]	0·21	0·21	0·18	0·18	0·74	0·74
5461	0·29	0·29	0·24	0·24	0·90	0·90
5086	0·45	0·43	0·36	0·34	1·17	1·16
4800	0·61	0·61	0·44	0·44	1·42	1·43
4358	1·05	1·07	0·78	0·78	2·13	2·13
4047	1·72	1·70	1·21	1·21	2·99	2·99
ψ-Yohimbone	*c* 0·9565; 20°.		*c* 0·9275; 21°		*c* 0·8108; 22°	
6438	−0·72	−0·72	−0·51	−0·48	−0·69	−0·65
5893	0·93	0·93	0·65	0·65	0·87	0·88
5780 [b]	1·00	0·99	0·70	0·70	0·94	0·94
5461	1·18	1·19	0·85	0·86	1·12	1·14
5086	1·53	1·51	1·14	1·14	1·47	1·47
4800	1·85	1·85	1·45	1·45	1·82	1·83
4358	2·71	2·71	2·23	2·23	2·74	2·74
4047	3·72	3·76	3·22	3·23	3·88	3·87

[a] As the sulphate. [b] Optical mean of doublet. [c] No readings taken. [d] Neither yohimbane sulphate nor yohimbane hydrochloride is soluble in water. [e] As hydrochloride in water; the sulphate is only sparingly soluble in water.

Results and Discussion

Yohimbine and its derivatives have ultraviolet absorption maxima at about 282 mμ, 256 mμ, and shorter wavelengths,[6 12] so that the squares of the constant wavelengths in the Drude terms describing the dispersion would be expected to be (in $m\mu^2 \times 10^{-6}$) about 0·08, 0·05, or 0·00. Graphs of $1/\alpha$ against λ^2 showed that, with one exception discussed below, the dispersions required either more than one Drude term, or in a few cases, a single term with an unsuitable value for the constant wavelength. In every case the dispersion could be described by an equation of the type

$$[M] = A/(\lambda^2 - 0{\cdot}08) + B/\lambda^2$$

Thus A represents an approximate measure of the contribution from the bands with $\lambda_{max.}$ *ca.* 280 mμ (*i.e.*, the long-wavelength indole band, or in the cases of the ketones, the sum of the contributions of this band and the carbonyl band), and B is the sum of the contributions from bands with absorption maxima at shorter wavelengths. A and B were determined so that the calculated values of the optical rotation, rounded off to the nearest hundredth of a degree, should agree with the experimental ones at two wavelengths—one each from the two groups 5893 or 5780 Å, and 4358, 4800, or 5086 Å (the wavelengths in each group are listed in order of decreasing preference)—and the sum of the squares of the errors at the other wavelengths should be a minimum. Table 1 shows the observed and calculated rotations, and Table 2 the values of A and B used; these are quoted to 4 or 5 figures because these numbers of digits were used in the calculations. However, the values of A and B are sensitive to changes in the constant wavelength used (particularly if A and B have opposite signs), and digits beyond the second have no stereochemical significance. In calculating A and B it was assumed that the constant wavelength would be the same for all compounds, and independent of the solvent; this is not strictly true,[13] but the errors introduced by this simplification are less than the experimental uncertainties.

The exception mentioned above was yohimbine in solution as its sulphate in water; here the dispersion could be accurately described by the equation $[M] = 119{\cdot}3/(\lambda^2 - 0{\cdot}053)$, implying that the only active band in the near ultraviolet region was that with $\lambda_{max.}$ 226 mμ. When the two-term equation above is used, for each compound A becomes more negative as the polarity of the solvent decreases; this regularity would be destroyed by using the single-term equation for yohimbine in water, as would the near-constancy of the change in A due to inversion at position 3 in yohimbine. Consequently the apparent simplicity of the dispersion of the yohimbinium cation is considered spurious.

Table 2. *Values of A and B in the equation* $[M] = A/(\lambda^2 - 0{\cdot}08) + B/\lambda^2$.

Base	Solvent	A	B	Base	Solvent	A	B
Yohimbine	Water	+57·31	+66·45	ψ-Yohimbine	Water	−69·520	+76·889
	Methanol	+34·69	+32·77		Methanol	−74·063	+76·473
	Chloroform	+16·82	−18·24		Chloroform	−90·097	+59·180
Yohimbone	Water	−6·67	−26·25	ψ-Yohimbone	Water	−68·286	+38·985
	Methanol	−25·57	−42·80		Methanol	−73·312	+59·449
	Chloroform	−67·38	−8·999		Chloroform	−89·316	+61·470
Yohimbane	Methanol	+5·635	−82·04				
	Chloroform	−4·462	−72·59				

The results show that the inversion of position 3 in yohimbine (3α-H ⟶ 3β-H) changes A by -117 ± 10, while B changes in the opposite sense. The change in A is responsible for the change in sign of the optical rotation for visible light on conversion of yohimbine into ψ-yohimbine, though the molecular rotation differences for the D-line, *viz.*, −440° in water, −280° in methanol, and −173° in chloroform are more variable than the changes in A. The low values for the specific rotation of ψ-yohimbine are due to the near cancellation of two large terms of opposite sign. This point is particularly clear in the case

[12] Jost, *Helv. Chim. Acta*, 1949, **32**, 1297.
[13] Djerassi and Closson, *J. Amer. Chem. Soc.*, 1956, **78**, 3761.

of ψ-yohimbine in pyridine; the results are not sufficiently accurate for detailed presentation, but the specific rotation has a maximum value of about +31 at *ca.* 540 mμ, then decreasing to zero and changing sign at about 415 mμ.

In the cases of yohimbone and ψ-yohimbone the values of A are the sums of the contributions from the indole and carbonyl bands. An approximate value for the contribution of the carbonyl band in yohimbone can be obtained by assuming that $A = A$ (for yohimbane) + A (carbonyl), whence A (carbonyl) is of the order of −50. If the sign of the latter is assumed to be solvent-independent, the low value of A for yohimbone in water could then arise from a lævorotatory carbonyl band and an indole band that is dextrorotatory as in yohimbine, and by extrapolation, in yohimbane. However, the values of A for ψ-yohimbine and ψ-yohimbone are nearly the same, and the differences between the specific rotations of the two compounds are due to the different values of B.

On conversion of yohimbone into yohimbane the numerical value of A decreases, and the dispersion in the visible region of the spectrum is determined chiefly by the contributions from the absorption bands with maxima at short wavelengths. The figures in Table 2 suggest that the specific rotation of yohimbane in methanol changes sign at about 293 mμ.

This work was done during the tenure of an I.C.I. Fellowship, for which I thank the University of Leeds.

Organic Chemistry Department, Leeds University. [*Received, March 26th*, 1959.]

NOTES.

616. *Synthesis of* 2,7-*Bis*-p-*hydroxyphenyl*-2,7-*dimethyloctane*.

By A. C. Davis and R. F. Hunter.

2,7-Bis-*p*-hydroxyphenyl-2,7-dimethyloctane (I) was required to ascertain the effect of lengthening the hydrocarbon bridge on the physical properties of cured resins obtained from its diglycidyl ether, in comparison with the dihydroxydiphenylpropane (II). The diacetylene (III) was prepared by condensing 2,7-dimethylocta-3,5-diyne-2,7-diol with phenol in the presence of phosphoric acid and also from *p*-1,1-dimethylprop-2-ynylphenol (IV) [obtained in very poor yield by condensation of 2-ethynylpropan-2-ol with phenol (cf. Nazarov and Kuynetsova [1])] by oxidation with oxygen in the presence of cuprous and ammonium chloride.

(I) Ar·CMe$_2$·[CH$_2$]$_4$·CMe$_2$·Ar Ar$_2$CMe$_2$ (II).

(III) Ar·CMe$_2$·C≡C·C≡C·CMe$_2$·Ar Ar·CMe$_2$·C≡CH (IV)

Ar = *p*-C$_6$H$_4$·OH

Reduction of the diacetylene with hydrogen in the presence of palladium–charcoal yielded the required compound (I). Its constitution was confirmed by synthesis from 2,7-dimethyloctane-2,7-diol and phenol. On condensation with epichlorohydrin in ethanol, with gradual addition of aqueous sodium hydroxide, it yielded the diglycidyl ether, which had the expected properties.

Experimental.—2,7-*Bis*-p-*hydroxyphenyl*-2,7-*dimethylocta*-3,5-*diyne* (III). (i) A mixture of 2,7-dimethyl-3,5-octadiyne-2,7-diol (200 g.), phenol (1 kg.), and phosphoric acid (*d* 1·71, 200 c.c.) was stirred at 60° for 3 hr., then diluted with water, and the organic layer was washed with water. The solvent and unchanged phenol were removed in steam, the reside cooled, and the aqueous layer was decanted and discarded. The crude resinous bisphenol was dissolved in a solution of potassium hydroxide (140 g.) in water (400 c.c.), added to 10% aqueous sodium hydroxide (2·5 l.), and kept for 3 hr. at room temperature. The precipitate sodium salt was collected, washed with a small amount of water, and treated with an excess of cold dilute hydrochloric acid under a layer of ether. The ethereal solution was washed with water, dried (K_2CO_3),

[1] Nazarov and Kuynetsova, *Bull. Acad. Sci. U.R.S.S., Cl. Sci. chim.*, 1942, 392; *Chem. Abs.*, 1945, **39**, 1620.

XUM

and concentrated under reduced pressure to a partially crystalline residue, which on recrystallisation from toluene (1 l.) gave the bisphenol (90 g., 23% crude yield) in two crops, m. p. 134—137° and 131—133°. For analysis a sample was recrystallised from ethylene dichloride and thereafter several times from 50% acetic acid to give the pure *bisphenol* in needles, m. p. 150—152° (Found: C, 83·25; H, 7·2. $C_{22}H_{22}O_2$ requires C, 83·0; H, 7·0%).

Treatment of the sodium salt of the bisphenol in water with benzoyl chloride gave the *dibenzoate*, which crystallised from ethyl acetate in leaflets, m. p. 200—201° (Found: C, 82·3; H, 5·6. $C_{36}H_{30}O_4$ requires C, 82·1; H, 5·7%).

(ii) Considerable difficulty was experienced in preparing *p*-1,1-dimethylprop-2-ynylphenol by condensation of 2-ethynylpropan-2-ol with phenol.[1] The acetylenic phenol was finally obtained in 3% yield only, as an oil of 30% concentration (estimated by hydrogenation) which did not give correct analytical figures. The presence of an ethynyl group was verified by the formation of a silver derivative. The alternative method of alkylation of phenol with isopropenylacetylene in presence of phosphoric acid surprisingly yielded *p*-t-pentylphenol (6%) as the only non-resinous phenolic product, m. p. 90° (Found: C, 80·4; H, 9·8. Calc. for $C_{12}H_{16}O$: C, 80·4; H, 9·8%). The benzoyl derivative had m. p. 58—59°. Huston and Hsieh [2] reported m. p.s 94—95° and 60—61° respectively.

The crude dimethylpropynylphenol (3·2 g.) was shaken under oxygen with a solution of cuprous chloride (5 g.) and ammonium chloride (8 g.) in water (20 c.c.) and ethanol (10 c.c.) until an excess of oxygen had been absorbed. The ethanol was distilled in a vacuum, and ether and dilute sulphuric acid were added. The product, isolated by washing and concentration of the ethereal solution, was a viscous brown oil (3·0 g.) giving no precipitate with silver nitrate solution. This was purified through the sodium salt to give an oil (1·2 g.) which after a single crystallisation from 60% acetic acid yielded 2,7-bis-*p*-hydroxyphenyl-2,7-dimethylocta-3,5-diyne (0·32 g.), m. p. 145—152°, undepressed on admixture with the specimen obtained in (i).

2,7-*Bis*-p-*hydroxyphenyl*-2,7-*dimethyloctane*.—(i) 2,7-Bis-*p*-hydroxyphenyl-2,7-dimethylocta-3,5-diyne (71 g.) in ethanol (250 c.c.) was shaken under hydrogen with 5% palladium charcoal (5 g.) until 22·1 l. had been absorbed. Evaporation of the filtered solution and crystallisation from 50% acetic acid (850 c.c.) gave pale brown leaflets (58·3 g.) which were dried to constant weight at 100°/0·5 mm. (m. p. 125—128°). An analytical sample of the *bisphenol* obtained after several recrystallisations from toluene and drying at 90°/10^{-5} mm. had m. p. 137—138° (Found: C, 81·8; H, 9·4. Calc. for $C_{22}H_{30}O_2$: C, 80·9; H, 9·3. $C_{22}H_{30}O_2,\frac{1}{2}C_7H_8$ requires C, 82·2; H, 9·2%). Analytical samples prepared by crystallisation from aqueous acetic acid gave consistently low microanalytical figures for carbon even after drying in a high vacuum near the m. p. (cf. Davis, Hayes, and Hunter [3]). The *dibenzoate*, prepared by a Schotten–Baumann reaction, crystallised from ethyl acetate in prisms, m. p. 191—192° (Found: C, 80·85; H, 6·9. $C_{36}H_{38}O_4$ requires C, 80·9; H, 7·2%). The diglycidyl ether was prepared by addition in small portions during 3½ hr. of sodium hydroxide (16·8 g.) in water (17 c.c.) to a stirred solution of the bisphenol (58·3 g.) in 95% ethanol (27 c.c.) and epichlorohydrin (99 g.) in a constant-temperature bath at 60°. Stirring was continued for a further ½ hr., the solvents were evaporated under reduced pressure at 60°, and water (75 c.c.) and toluene (60 c.c.) were added. After being washed with water, the organic layer was concentrated under reduced pressure, finally at 100°/0·5 mm.; the diglycidyl ether formed a viscous clear brown liquid which was not further purified and gradually crystallised (n_D^{17} 1·5492) (Found: epoxide equiv., 254. Calc., 219). (ii) 2,7-Dimethyloctane-2,7-diol (3·5 g., 0·02 mole) was boiled in phenol (37·6 g., 0·4 mole) with zinc chloride (5·5 g.) for 8 hr. and unchanged phenol removed in steam. The ethereal solution obtained on treatment of the residue with ether and dilute hydrochloric acid was washed with water and extracted with 10% aqueous potassium hydroxide. Saturation of the alkaline extract with carbon dioxide gave a brown gum (0·3 g.) which on purification through a solid sodium salt, neutralisation with carbon dioxide, and crystallisation from 40% acetic acid gave the bisphenol in plates, m. p. 130° after sintering and 132—134° when mixed with the specimen described in (i). The oily residue (3·6 g.) recovered from the ethereal solution, on distillation at 130°/10^{-5} mm., gave a *product* as a viscous yellow oil, n_D^{15} 1·5338 (Found: C, 83·3; H, 10·7. $C_{16}H_{24}O$ requires C, 82·7; H, 10·4%).

RESEARCH AND DEVELOPMENT DEPARTMENT, BAKELITE LIMITED,
TYSELEY, BIRMINGHAM, 11. [*Received, January 15th*, 1959.]

[1] Huston and Hsieh, *J. Amer. Chem. Soc.*, 1936, **58**, 439.
[2] Davis, Hayes, and Hunter, *J. Appl. Chem.*, 1953, **3**, 312; 1957, **7**, 521.

617. *Nitrogenous Chelate Complexes of Transition Metals. Part II.*[1] *The Tervalent Gold Complexes of 2,2′-Bipyridyl.*

By C. M. Harris and T. N. Lockyer.

Tervalent gold complexes of 1,10-phenanthroline (phen) have been recently examined in nitrobenzene and acetone solutions by means of conductometric and spectrophotometric measurements.[1] The rapid reaction of halide ions (*i.e.*, Cl^- and Br^-) with the dihalogeno-(1,10-phenanthroline)gold(III) ion proceeds virtually to completion in these solvents, thus:

$$[Au(phen)X_2]^+ + 2X^- \longrightarrow [AuX_4]^- + phen$$

An explanation of this phenomenon, as well as the marked difference in colour between the simple halides, $[Au(phen)X_2]X$, and the corresponding perchlorates, $[Au(phen)X_2]ClO_4$, has been given in terms of the ability of tervalent gold, under suitable conditions, to utilise two additional $6p6d$ bonds perpendicular to its normal $5d6s6p^2$ square planar arrangement. The reactions of the 2,2′-bipyridyl complexes of gold(III) have since been shown to be similar to those of 1,10-phenanthroline, and the preparations and properties of these compounds are briefly reported here.

Block and Bailar [2] have previously reported the isolation of the dihalogeno-(2,2′-bipyridyl)gold(III) ions as their tetrahalogenoaurate(III) derivatives, $[Au(bipy)X_2][AuX_4]$ (bipy = 2,2′-bipyridyl; X = Cl, Br), as well as an impure specimen of $Au(bipy)Cl_3$. The pure chloride $Au(bipy)Cl_3$ has now been isolated from aqueous solution, as well as the compounds $[Au(bipy)X_2]ClO_4$ (where X = Cl, Br) and [bipy H]$[AuX_4]$ (X = Cl, Br). Attempts to isolate the simple bromide $Au(bipy)Br_3$ were unsuccessful. The dichloro-(2,2′-bipyridyl)gold(III) ion is hydrolysed in aqueous solution, and the hydroxy-chloro-(2,2′-bipyridyl)gold(III) ion was isolated as the perchlorate $[Au(bipy)Cl(OH)]ClO_4$. It is noteworthy that Bjerrum [3] has reported that the $[AuCl_4]^-$ ion undergoes a slow hydrolysis, forming the $[AuCl_3OH]^-$ species. Attempts to prepare analogous iodo-complexes were unsuccessful. The black insoluble tetraiodoaurate(III) complex $[N(Et)_4][AuI_4]$ was obtained but it decomposed in solution and was not further investigated.

The molecular conductivities of these compounds both in nitrobenzene and in nitromethane solution are listed in the Table. The chloro-complex $Au(bipy)Cl_3$ exhibits conductivities in these solvents of the order expected for rearrangement to $[Au(bipy)Cl_2][AuCl_4]$, as has been previously observed for the analogous 1,10-phenanthroline complex in nitrobenzene or acetone. This was confirmed by conductometrically titrating the perchlorate $[Au(bipy)Cl_2]ClO_4$ (5×10^{-4}M) with methyltriphenylarsonium chloride (10^{-2}M) in nitrobenzene, a sharp end-point corresponding to the addition of two chloride ions being observed. A similar result was obtained for the titration of $[Au(bipy)Br_2]ClO_4$ with $[N(Et)_4]Br$ in nitromethane.

Spectrophotometric measurements were made on the chloro-complexes in nitromethane solution (see Fig. 1) in the range 5500—3750 Å. Although these compounds exhibit no definite absorption maxima in this region, it can be seen that the curve for 10^{-3}M-$[Au(bipy)Cl_2][AuCl_4]$ is practically identical with the composite curve constructed from those for 10^{-3}M-$[Au(bipy)Cl_2]ClO_4$ and 10^{-3}M-$Na[AuCl_4],2H_2O$. The curve for 2×10^{-3}M-$[Au(bipy)Cl_2]Cl$ is the same as that for 10^{-2}M-$[Au(bipy)Cl_2][AuCl_4]$, as expected for the postulated equilibrium. The bromo-complexes were also examined in this solvent (see Fig. 2), and it can be seen that the curve for 5×10^{-4}M-$[Au(bipy)Br_2][AuBr_4]$ is practically identical with the composite curve constructed from 5×10^{-4}M-$[Au(bipy)Br_2]ClO_4$ and $[N(Et)_4][AuBr_4]$.

[1] Part I, Harris, *J.*, 1959, 682.
[2] Block and Bailar, *J. Amer. Chem. Soc.*, 1951, **73**, 4722.
[3] Bjerrum, *Bull. Soc. chim. Belg.*, 1948, **57**, 432.

Molecular conductivities (mho) of gold(III)–2,2′-bipyridyl complexes in 10^{-3}M-nitrobenzene and -nitromethane at 25°.

Compound	In $PhNO_2$	In $MeNO_2$	Compound	In $PhNO_2$	In $MeNO_2$
$[Au(bipy)Cl_2]Cl$	14·4	43·7	$[Au(bipy)Br_2]ClO_4$	—	94·0
$[Au(bipy)Cl_2]ClO_4$	29·0	88·6	$[Au(bipy)Br_2][AuBr_4]$ ...	—	86·5
$[Au(bipy)Cl(OH)]ClO_4$ ...	29·5	92·0	$[N(Et)_4][AuBr_4]$	32·8	96·0
$[Au(bipy)Cl_2][AuCl_4]$	28·8	87·3	[bipy H][$AuBr_4$]	30·8	89·7
[bipy H][$AuCl_4$]	31·1	87·5			

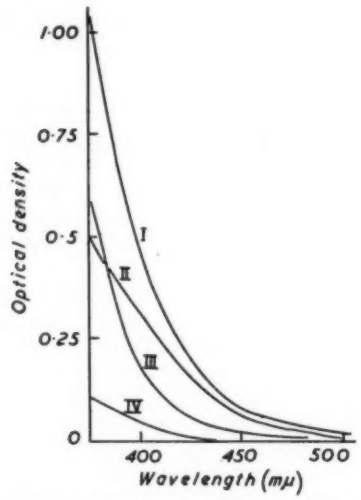


FIG. 1. *Absorption spectra of the chloro-complexes in nitromethane* (1 *cm. cell*).

I Observed curve for 10^{-3}M-$[Au(bipy)Cl_2][AuCl_4]$, also for 2×10^{-3}M-$[Au(bipy)Cl_2]Cl$, also composite curve from addition of II and III.
II 10^{-3}M-$Na[AuCl_4],2H_2O$.
III 10^{-3}M-$[Au(bipy)Cl_2]ClO_4$.
IV 10^{-3}M-$[Au(bipy)Cl(OH)]ClO_4$.

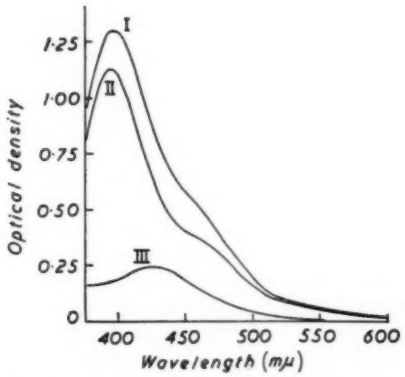


FIG. 2. *Absorption spectra of the bromo-complexes in nitromethane* (1 *cm. cell*).

I 5×10^{-4}M-$[Au(bipy)Br_2][AuBr]$, also composite curve from addition of II and III.
II 5×10^{-4}M-$[NEt_4][AuBr_4]$.
III 5×10^{-4}M-$[Au(bipy)Br_2]ClO_4$.

Experimental.—Dichloro-(2,2′-bipyridyl)gold(III) *chloride.* To a boiling solution of 2,2′-bipyridyl (0·65 g.) in water (10 ml.) was added $Na[AuCl_4],2H_2O$ (0·80 g.) in water (10 ml.) with stirring. The yellow precipitate of $[Au(bipy)Cl_2][AuCl_4]$, which was first deposited, dissolved on boiling for a few minutes. Lithium chloride (5 g.) was stirred in and the clear solution was left overnight in the refrigerator. The orange needles were washed with a large excess of anhydrous acetone followed by anhydrous ether (yield of vacuum-dried *salt*, 0·35 g.) (Found: C, 25·8; H, 1·6; N, 5·8; Au, 42·4. $C_{10}H_8N_2Cl_3Au$ requires C, 26·1; H, 1·75; N, 6·1; Au, 42·8%).

Dichloro-(2,2′-bipyridyl)gold(III) *perchlorate.* To a boiling aqueous solution of $[Au(bipy)Cl_2]Cl$, prepared as above, excess of 75% perchloric acid was added dropwise, with stirring. The solution was cooled, and the pale yellow crystals were filtered off and washed in turn with water, ethanol, and ether (Found: C, 23·2; H, 1·7; N, 5·3; Au, 37·7%. $C_{10}H_8O_4N_2Cl_3Au$ requires C, 22·9; H, 1·5; N, 5·4; Au, 37·6%).

Hydroxy-chloro-(2,2′-bipyridyl)gold(III) *perchlorate.* To a boiling solution of $Na[AuCl_4],2H_2O$ (0·20 g.) and 2,2′-bipyridyl (0·26 g.) in water (20 ml.) was added dropwise a hot solution of sodium perchlorate (2·0 g.) in water (10 ml.). The pale cream *compound* was washed with water, ethanol, and ether (yield, 0·24 g.) (Found: C, 23·7; H, 1·8; N, 5·5; Au, 39·0; Cl, 7·3. $C_{10}H_9O_5N_2Cl_2Au$ requires C, 23·9; H, 1·8; N, 5·6; Au, 39·0; Cl, 7·0%).

Dichloro-(2,2′-bipyridyl)gold(III) *tetrachloroaurate*(III). This compound was prepared by treating 2,2′-bipyridyl dropwise with a hot aqueous solution of $Na[AuCl_4],2H_2O$. The yellow compound was washed with water, ethanol, and ether (Found: C, 16·2; H, 1·05; N, 3·8; Au, 51·6. Calc. for $C_{10}H_8N_2Cl_6Au_2$: C, 15·7; H, 1·1; N, 3·7; Au, 51·6%).

2,2′-Bipyridylium tetrachloroaurate(III). Sodium tetrachloroaurate(III) dihydrate (0·40 g.) in M-hydrochloric acid (20 ml.) was added to 2,2′-bipyridyl (0·16 g.) in M-hydrochloric acid (20 ml.). The yellow *salt* was precipitated immediately; it was washed with water, ethanol, and ether (yield, 0·35 g.) (Found: C, 24·5; H, 1·8; N, 5·7; Au, 39·5. $C_{10}H_9N_2Cl_4Au$ requires C, 24·2; H, 1·8; N, 5·7; Au, 39·8%).

Dibromo-(2,2′-bipyridyl)gold(III) *tetrabromoaurate*(III). This compound was prepared in an analogous manner to the corresponding chloro-complex from a solution of $Na[AuBr_4]$ (Found: C, 11·9; H, 1·0; N, 2·7; Au, 38·3. Calc. for $C_{10}H_8N_2Br_6Au_2$: C, 11·7; H, 0·8; N, 2·7; Au, 38·3%).

Dibromo-(2,2′-bipyridyl)gold(III) *perchlorate*. $[Au(bipy)Br_2][AuBr_4]$ (0·5 g.) was dissolved in boiling water (600 ml.) in the presence of 2,2′-bipyridyl (0·15 g.). The solution was filtered hot to remove some undissolved starting material and 75% perchloric acid (10 ml.) was added to the hot solution. Crystallisation began almost immediately, and after cooling, the golden crystals were washed in turn with cold water, ethanol, and anhydrous ether (yield of vacuum-dried *perchlorate*, 0·44 g.) (Found: C, 19·6; H, 1·45; N, 4·6; Au, 32·1. $C_{10}H_8O_4N_2ClBr_2Au$ requires C, 19·6; H, 1·3; N, 4·6; Au, 32·2%).

Tetraethylammonium tetrabromoaurate(III). This compound was prepared by Harris's method [1] (Found: Au, 30·2. Calc. for $C_8H_{20}NBr_4Au$: Au, 30·4%).

2,2′-Bipyridylium tetrabromoaurate(III). This *compound* was prepared in an analogous manner to the tetrachloro-derivative (Found: C, 17·5; H, 1·4; N, 4·1; Au, 29·1. $C_{10}H_9N_2Br_4Au$ requires C, 17·8; H, 1·35; N, 4·2; Au, 29·2%)

Tetraethylammonium tetraiodoaurate(III). $Na[AuCl_4],2H_2O$ (0·5 g.) in water (20 ml.) was added slowly to a large excess of potassium iodide (4·0 g.) in water (20 ml.). The dark solution was filtered, and to it was added a solution of tetraethylammonium iodide (0·4 g.) in water (25 ml.), slowly with stirring. The black *salt* was precipitated immediately; it was washed with water and dried over P_2O_5 *in vacuo* at 80° (yield, 1·00 g.) (Found: C, 11·8; H, 2·2; N, 1·7; Au, 23·6. $C_8H_{20}NI_4Au$ requires C, 11·5; H, 2·4; N, 1·7; Au, 23·6%).

Physical measurements. The spectra were recorded on a Cary 11-Ms-50 Spectrophotometer. The nitromethane and nitrobenzene were purified as described elsewhere.[4]

We thank Dr. E. Challen for micro-analyses (C,H,N) and Mr. I. Reece for spectrophotometric measurements. One of us (T. N. L.) thanks I.C.I.A.N.Z. for a research fellowship.

Department of Inorganic Chemistry,
University of New South Wales,
Broadway, Sydney, Australia. [*Received, February 3rd*, 1959.]

[4] Harris, Livingstone, and Reece, *J.*, 1959, 1505.

---

618. *Interaction of Tetranitromethane with Aromatic Hydrocarbons.*

By (Miss) Jayanti Nag Chaudhuri and Sadhan Basu.

Macbeth [1] has shown that the red colour produced by ethylenic compounds with tetranitromethane is much less intense with conjugated compounds, especially with aromatic hydrocarbons. Nitro-compounds in general are good electron-acceptors and form molecular complexes of charge-transfer type with electron donors.[2] As aromatic compounds are good electron donors they should form molecular complexes with tetranitromethane. With this in view the present investigation was undertaken.

Experimental.—Tetranitromethane, 99% pure, supplied by L. Light & Co., in water, chloroform, and carbon tetrachloride, showed a characteristic absorption band in the range 270—280 mμ, which corresponds well with the 275 mμ band observed for the vapour.[3] In normal

[1] Macbeth, *J.*, 1915, **107**, 1826; Harper and Macbeth, *J.*, 1915, **107**, 87.
[2] Mulliken, *J. Amer. Chem. Soc.*, 1952, **74**, 811.
[3] Nicholson, *J.*, 1949, 1555.

XUM

heptane, however, it showed a general absorption with no characteristic maximum in the region of 200—400 mμ. Evans [4] observed a similar spectrum in cyclohexane and attributed it to contact charge-transfer interaction.

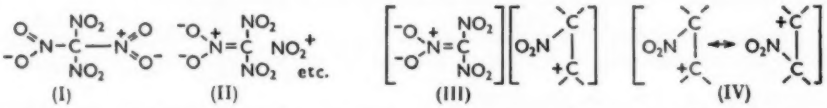
The solvents used were E. Merck's spectroscopically pure samples and were used without further purification. Polynuclear hydrocarbons, supplied by B.D.H. and L. Light & Co., were purified by chromatography on alumina from neutral solvents and subsequent recrystallisation. The purified samples were >99% pure, as shown by their extinctions at the characteristic absorption maxima in ethanol.

Spectral measurements were made in a Beckman Spectrophotometer Model DU with 5 cm. silica cells. Above 320 mμ tetranitromethane in the concentration range used in the present series of measurements gave 100% transmission. The measurements with mixtures of hydrocarbons and tetranitromethane were made with a balancing solution containing the hydrocarbon in the same concentration as in the mixture.

The Table shows the characteristic absorption maximum (in mμ) of systems containing tetranitromethane (10^{-4}M) and nine polynuclear aromatic hydrocarbons (0·01M) in chloroform. The value of $h\nu$ (in ev) corresponding to these wavelengths, and ionisation potentials I.P. (in volts) of these hydrocarbons were calculated by the molecular orbital method.[5]

Compound	λ	$h\nu$	I.P.	Compound	λ	$h\nu$	I.P.
Naphthalene	359	3·46	8·30	Triphenylene	397	3·28	8·48
Anthracene	407	3·05	7·74	Biphenyl	330	3·76	8·53
Phenanthrene	390	3·18	8·27	Stilbene	405	3·07	7·99
Chrysene	397	3·13	8·04	Fluoranthene	416	2·98	8·30
Pyrene	388	3·20	7·82				

Discussion.—The peaks of the absorption band of tetranitromethane–olefinic systems usually appear in the range of 450—500 mμ. It is evident from the Table that the band for tetranitromethane–aromatic hydrocarbons lies at much shorter wavelengths, although from the consideration of ionisation potentials of ethylene (10 v) and the aromatic hydrocarbons the band for the latter should appear at much longer wavelengths. This suggests that the tetranitromethane undergoes interaction with olefinic compounds which is not of charge-transfer type. Patterson [6] represented tetranitromethane by means of a resonance hybrid of the covalent (I) and ionic structures (II). He represented the tetranitromethane



(I) (II) (III) (IV)

complex of ethylenic compounds by structures of the type (III) and attributed the visible colour to charge resonance in the ion (IV). We suggest that for ethylenic compounds the colour is due to charge-resonance absorption, while for aromatic hydrocarbons the absorption is of charge-transfer type. But this does not mean that the interaction of the type (III) and (IV) cannot take place with aromatic hydrocarbons. In fact Maatman and Rogers [7] noted absorption in the region 400—500 mμ with polynuclear aromatic hydrocarbons, using somewhat higher tetranitromethane concentrations; this is probably the charge-resonance band. That tetranitromethane undergoes heteropolar dissociation in systems containing polynuclear aromatic hydrocarbons is shown by the following observations.

The complex-forming reaction of tetranitromethane with aromatic hydrocarbons was found to be time-dependent. This did not interfere with the location of the characteristic charge-transfer band but accurate measurement of optical density was not possible. For tetranitromethane–anthracene the 407 mμ band increased in intensity at first rapidly, then more slowly. After about a week the peak at 407 mμ had been completely replaced by a more

[4] Evans, *J.*, 1957, 4232.
[5] Bhattacharya and Basu, *Trans. Faraday Soc.*, 1958, **54**, 1286.
[6] Patterson, *J. Org. Chem.*, 1955, **20**, 1277.
[7] Maatman and Rogers, Amer. Chem. Soc. Div. Petroleum Chem., Gen. Papers, 1955, No. **33**, pp. 5—11.

intense band at 365 mμ. The absorption spectrum of the system at this stage resembled that of 9-nitroanthracene fairly closely,[8] indicating nitration of the anthracene nucleus. Similarly, the absorption spectrum of tetranitromethane–naphthalene resembled that of α-nitronaphthalene after about a week. Nitration of hydrocarbons by tetranitromethane [6] has also been observed by previous workers, but the present investigation shows that it is preceded by charge-transfer interaction. Since nitration involves the NO_2^+ radical, it is evident that the ionic structure (II) of the tetranitromethane must also participate in the interaction of tetranitromethane with aromatic hydrocarbons. Charge resonance of the type (IV) has not been observed by us, probably because of the low concentration of the constituents.

We thank Professor R. S. Mulliken and one of the referees for helpful criticism, and the Council of Scientific & Industrial Research, India, for a Junior Research Fellowship (to J. N. C.).

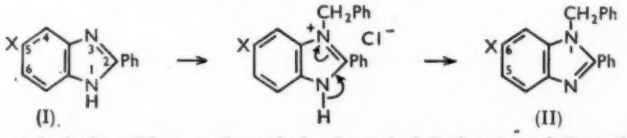
Department of Chemistry, University College of Science & Technology,
Calcutta-9, India. [*Received, February 16th*, 1959.]

[8] Jones, *Chem. Rev.*, 1947, **41**, 353.

619. *Benzylation of 2-Phenylbenzimidazoles.*

By N. V. Subba Rao and C. V. Ratnam.

Hinsberg,[1] heating 5-methyl-2-phenylbenzimidazole (I; X = Me) at 160° with benzyl chloride and benzene, obtained the *N*-benzyl derivative, but did not determine whether the methyl group was in the 5- or the 6-position. We have benzylated 5-methyl-, 5-chloro-, and 5-nitro-2-phenylbenzimidazole, obtaining better yields by refluxing the benzimidazoles with benzyl chloride in the presence of fused sodium acetate and a trace of iodine. The products were characterised by comparison with synthetic samples.[2,3,4] 5-Methyl-2-phenylbenzimidazole gave 1-benzyl-6-methyl- whereas 5-chloro-2-phenylbenzimidazole yielded 1-benzyl-5-chloro-2-phenylbenzimidazole. The 5-nitrobenzimidazole, on the other hand, gave a 2 : 1 mixture of 5- and 6-nitro-compounds.



(I) (II)

Phillips,[5] methylating 5-bromo-2-methyl-, 2-methyl-5-nitro-, and 5-methyl-benzimidazole, found the Bz-substituent to be mainly in the 5- or the 6-position in the product according to the reagent used; 2 : 5-dimethylbenzimidazole, however, gave only the 1 : 2 : 5-compound.

Our results may be explained as follows: A benzimidazole having an electron-releasing group (*e.g.*, methyl) at position 5 will exist mainly in form (I) since the "*para-*"nitrogen atom will have a greater electron density for holding the proton; if the 5-substituent is an electron-withdrawing group (*e.g.*, chloro or nitro), the tautomer of structure (I) will be the major component. Benzylation in the absence of aqueous alkali may be expected to take place by the addition of a benzyl cation to the more basic, tertiary nitrogen atom, leading to the 6-substituted compound (II) from compound (I), and the 5-substituted isomer from its tautomer, as found for the methyl and chloro-derivatives. In the case of the nitrobenzimidazole the 5-nitro-compound is the major product, as expected; however,

[1] Hinsberg, *Ber.*, 1886, **19**, 2025.
[2] Rao and Ratnam, *Proc. Indian Acad. Sci.*, 1956, **44**, 331.
[3] *Idem, ibid.*, 1958, **47**, 77.
[4] *Idem, ibid.*, p. 81.
[5] Phillips, *J.*, 1931 1143.

owing to the deactivating influence of the nitro-group, the reaction is slowed down and form (I; X = NO_2), though the minor entity, is the more reactive and so some of the 6-nitro-isomer is also obtained.

Experimental.—Benzylation of 5-methyl-2-phenylbenzimidazole. The benzimidazole (1 g.), freshly fused sodium acetate (0·5 g.), redistilled benzyl chloride (2 ml.) and a speck of iodine were refluxed for 9 hr., then added to an excess of water with stirring. The resulting mass on trituration with ethanol gave a solid (0·8 g.) which, recrystallised from alcohol and then benzene, yielded prismatic rods of 1-benzyl-6-methyl-2-phenylbenzimidazole,[2] m. p. and mixed m. p. 195°. The alcoholic filtrate from the crude solid, on evaporation and repeated washing with light petroleum, gave a further 0·1 g. of the same compound.

Benzylation of 5-chloro-2-phenylbenzimidazole. The chlorobenzimidazole (0·5 g.) yielded the 1 : 2-disubstituted benzimidazole 1-benzyl-5-chloro-2-phenylbenzimidazole[3] (0·45 g.), prismatic rods (from alcohol), m. p. and mixed m. p. 170°.

Benzylation of 5-nitro-2-phenylbenzimidazole. The nitrobenzimidazole (0·5 g.) was benzylated as above. The crude product (0·45 g.) which was insoluble in aqueous potassium hydroxide had m. p. 140°. Chromatography over alumina with benzene as eluant gave a fraction, m. p. 185°, and benzene–alcohol gave a fraction, m. p. 159°. The higher- and the lower-melting compound were identical with the 6- and the 5-nitro-isomer,[4] respectively. By repeated chromatography, the 5- and the 6-nitro-isomer were obtained in the ratio of 2 : 1.

We thank Professor T. R. Seshadri of Delhi University for discussions of the mechanism.

OSMANIA UNIVERSITY, HYDERABAD-7, DECCAN, INDIA. [*Received, February 23rd,* 1959.]

---

620. *The Dissociation Constant of Fluorine.*

By A. F. TROTMAN-DICKENSON.

DOESCHER[1] measured the dissociation of fluorine in a static system and expressed his observations of the equilibrium

$$F_2 = 2F$$

by the equation

$$\ln K \text{ (in atmospheres)} = 14{\cdot}5 - 19000/T,$$

where T is the absolute temperature. Stamper and Barrow[2] analysed Doescher's results by a third-law treatment and found that $\Delta H^\circ_0 = 36{\cdot}71 \pm 0{\cdot}13$ kcal. mole^{-1}. Although Doescher's equation satisfactorily represents his observations, it is not suitable for lengthy extrapolations. The Table below lists equilibrium constants that have been calculated

Temp. (° K)	log $K_{obs.}$	log K_d	log K_c	log (K_d/K_c)	Temp. (° K)	log $K_{obs.}$	log K_d	log K_c	log (K_d/K_c)
100	—	$\bar{7}7{\cdot}777$	$\bar{7}6{\cdot}231$	−0·454	600	—	$\bar{3}{\cdot}545$	$\bar{3}{\cdot}364$	0·181
200	—	$\bar{3}5{\cdot}037$	$\bar{3}6{\cdot}831$	0·206	760	$\bar{3}{\cdot}34$	$\bar{3}{\cdot}440$	$\bar{3}{\cdot}342$	0·098
300	—	$\bar{2}2{\cdot}791$	$\bar{2}2{\cdot}501$	0·290	1112	$\bar{2}{\cdot}90$	$\bar{2}{\cdot}877$	$\bar{2}{\cdot}912$	−0·035
400	—	$\bar{1}1{\cdot}668$	$\bar{1}1{\cdot}399$	0·269	1500	—	0·796	0·902	−0·106
500	—	$\bar{1}1{\cdot}794$	$\bar{1}1{\cdot}570$	0·224	2000	—	2·172	2·364	−0·192

by the standard methods of statistical mechanics,[3] the new value of ΔH°_0 being used. The following physical constants of the fluorine molecule were used: $\omega_0 = 891{\cdot}8$ cm.$^{-1}$,[4] $x_e\omega_e = 15{\cdot}6$ cm.$^{-1}$,[5] $r_0 = 1{\cdot}418$ Å[4] (Stamper and Barrow incorrectly list r_0 as 1·442 Å). The deviations of the true values of the equilibrium constants from those of Doescher's

[1] Doescher, *J. Chem. Phys.*, 1952, **20**, 330.
[2] Stamper and Barrow, *Trans. Faraday Soc.*, 1958, **54**, 1592.
[3] Guggenheim and Prue, "Physicochemical Calculations," North Holland Publ. Co., Amsterdam, 1955.
[4] Andrychuk, *Canad. J. Phys.*, 1951, **29**, 151.
[5] Rees, *J. Chem. Phys.*, 1957, **26**, 1567.

equation are considerable. Intermediate values of the equilibrium constant between 100 and 2000° K can most simply be found from Doescher's equation by the application of a correction obtained by interpolation.

All equilibrium constants are in atmospheres. $K_{obs.}$ are the observed values, K_d those from Doescher's equation, and K_c those calculated by statistical mechanics.

DEPARTMENT OF CHEMISTRY, EDINBURGH UNIVERSITY. [*Received, March 4th, 1959.*]

---

621. *The Infrared Spectrum of a Platinous Complex having a Bridging Ethylenediamine Group with the* trans-*Configuration: [Bisethylene-tetrachloro-μ-ethylenediaminediplatinum*(II)].

By D. B. POWELL and N. SHEPPARD.

IN a recent study of the infrared spectra of chelated metal complexes of ethylenediamine, it has been shown that two types of infrared spectrum occur and it was suggested [1] that they may correspond to *gauche*- and *cis*-configurations of the ligand. It is therefore of interest to examine the spectrum of complexes where the ethylenediamine has the *trans*-configuration. A compound where this structure seems probable is the complex $(C_2H_4)PtCl_2NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2PtCl_2(C_2H_4)$ (I *), obtained by the addition of aqueous ethylenediamine to an aqueous solution of Zeise's salt, $KPt(C_2H_4)Cl_3,H_2O$.[2]

The absorption bands due to the ethylene group can be identified by comparison with the spectrum of *trans*-$Pt(C_2H_4)(NH_3)Cl_2$.[3] The remaining bands due to the ethylenediamine group (Figure, *b*) show an extremely simple spectrum,† which is in marked contrast to that of the chelated ethylenediamine complex, $Pt(en)Cl_2$ (Figure, *a*). In these spectra absorption peaks due to the ethylene group are marked "*e*" The simple spectrum obtained for the bridged complex (I) can be readily explained if the ethylenediamine group has the symmetrical *trans*-configuration.

The absorption bands which are not found in the simple ethylene complex, and which are therefore assigned to the ethylenediamine group, can be further differentiated by comparison with the spectrum of compound (II), in which the NH_2 groups of (I) are replaced by ND_2 (Figure, *c*). By using this method it is relatively easy to identify the vibrations associated primarily with $-NH_2$ vibrations and to arrive at a reasonable assignment of many of the absorption bands to fundamental vibrations in the molecule. The results obtained and the suggested assignments are listed in the Table, together with the absorption frequencies observed in the spectrum of *trans*-$Pt(C_2H_4)(NH_3)Cl_2$. The spectrum of the latter has been recorded previously.[3]

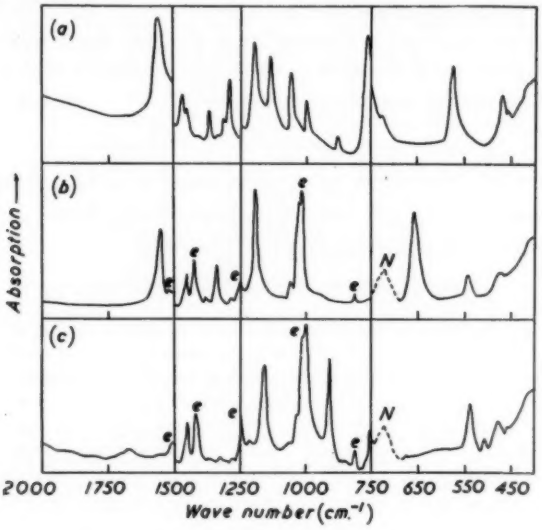
The frequency shifts due to deuteration of the NH_2 groups are mostly fairly obvious from the spectra in the Figure, *b* and *c*. However, the band centred at 1000 cm.$^{-1}$ in the deutero-compound (II) causes some confusion, as the absorption is made up of the band shifted from 1336 cm.$^{-1}$ in (I), superimposed on the doublet at 1023—1016 cm.$^{-1}$ due to the ethylene group. The absorption band at 653 cm.$^{-1}$ is undoubtedly due to an N–H deformation as shown by the marked frequency shift on deuteration, but the latter appears to be accompanied by a surprising reduction in intensity. It is possible that the assignments of the NH_2 twisting and NH_2 wagging modes should be interchanged. This would be preferable on intensity grounds, but less likely on the basis of the frequencies.

* This compound will be referred to subsequently as I, whereas the compound where the NH_2 groups have been replaced by ND_2, will be shown as II.

† It is suggested that this pattern of spectrum be provisionally described as type *C* to distinguish it from the more complex type *A* and type *B* spectra found previously for chelated ethylenediamine complexes.[1]

[1] Powell and Sheppard, *J.*, 1959, 791.
[2] Helman, *Compt. rend. Acad. Sci., U.R.S.S.*, 1943, **38**, 243.
[3] Powell, *J.*, 1956, 4459.

Infrared absorption spectra of (a) $Pt(en)Cl_2$, (b) (I), (c) *the deutero-compound* (II). 2000—1500 and 1250—400 cm.$^{-1}$, Nujol mull; 1500—1250 cm.$^{-1}$, hexachlorobutadiene; N = Nujol band.



A difficulty in the assignment of the CH_2 vibrations is caused by the weakness of the absorption bands compared with those from the NH_2 groups and the co-ordinated ethylene molecule. It is therefore difficult to distinguish absorption due to these vibrations from the stronger overtone and combination frequencies; there is also a considerable danger of these weak bands' being obscured by other strong absorptions. The CH_2 bending

Infrared absorption frequencies (cm.$^{-1}$) *of compounds* (I) *and* (II) *compared with those of* $Pt(C_2H_4)(NH_3)Cl_2$.

$Pt(C_2H_4)(NH_3)Cl_2$	(I)	(II)	νN–H/νN–D	Assignment *
	3265 s	2412 s	1·35	νN–H
Not investigated				
2045 w	2034 w	2032 w		*e*
	1551 s	1158 s	1·34	NH_2 bend
1520 vw	1520 vw	1520 vw		*e*
	1452 m	1450 m		CH_2 bend
1432, 1422 s	1421 m	1417 m		*e*
	1375 w	?		CH_2 wag?
	1336 m	1000 m	1·34	NH_2 wag
		1324 w		
	1280 w	1277 w		CH_2 twist
?(1250 in Zeise's salt)	1250 m	1251 m		*e*
	1190 s	912	1·31	NH_2 twist
	1118 vw	—		
	1052 w	?		ν skeletal
1023, 1010 s	1023, 1016 s	1026, 1013 s		*e*
980 vw	895 vw	880, 841 vw		
816 w	818 w	810 m		*e*
	?	752 w		CH_2 rock
691 m	712 vw	716 vw		*e*
Absorption peaks due to NH_3 group omitted	653 s	506 w	1·29	NH_2 rock
	540 w	537 m		νPt–N and skeletal bending
	475 w	475 w		

* "*e*" indicates that the peak is assigned to the ethylene group. Detailed assignments of the spectra of ethylene–platinum complexes have been discussed elsewhere.[4]

mode is fairly strong and easily distinguished, and the remaining CH_2 deformations may be expected to follow the usual order of frequencies for CH_2 angle deformation modes, as observed for n-butane [5] and for ethylenediamine itself,[6] namely, bend > wag > twist > rock; a skeletal vibration probably occurs near 1000 cm.$^{-1}$, by analogy with n-butane.[5] The band at 750 cm.$^{-1}$ in (II) appears to have no counterpart in (I). It seems probable that it is a CH_2 rocking frequency, the intensity of which is increased on deuteration of the NH_2 group.

The absorptions found from 600 to 450 cm.$^{-1}$ may arise either from skeletal bending modes of the ethylenediamine group, or from platinum–nitrogen stretching vibrations; there are two bands in this region, at 540 and 475 cm.$^{-1}$. In *trans*-$Pt(C_2H_4)(NH_3)Cl_2$,[3] the ν(Pt–N) vibration has been identified at 480 cm.$^{-1}$.

The characteristic spectrum associated with an ethylenediamine group having the *trans*-configuration should enable this structure to be identified in other ethylenediamine complexes. Evidence of the *trans*-configuration has been found for crystalline ethylenediamine dihydrochloride, but this somewhat different spectrum will be discussed elsewhere.

Experimental.—All spectra were obtained with a Hilger H 800 spectrometer, with rock-salt and potassium bromide prisms. The samples were examined as dispersions in liquid paraffin and hexachlorobutadiene.

Zeise's salt, $K[Pt(C_2H_4)Cl_3],H_2O$, was prepared as described by Chatt and Duncanson.[7] The ethylenediamine complex (I) was precipitated by the addition of aqueous ethylenediamine to the salt. The precipitate was centrifuged, washed, and dried *in vacuo* over phosphoric oxide.

The deutero-compound (II) was prepared by repeatedly evaporating a D_2O solution of ethylenediamine hydrochloride in a vacuum desiccator over phosphoric oxide, until spectroscopic examination showed that replacement of NH_2 by ND_2 was essentially complete. This deutero-derivative was then dissolved in 99·98% D_2O and added to a D_2O solution of Zeise's salt. On neutralisation of the solution with potassium carbonate, also in D_2O, the complex was precipitated; it was then washed with D_2O and dried overnight *in vacuo*.

Thanks are due to Imperial Chemical Industries Limited for financial assistance and particularly for the gift of the deuterium oxide.

Sir John Cass College, Jewry Street, London, E.C.3 (D. B. P.).
University Chemical Laboratory, Cambridge (N. S.). [*Received, March 11th*, 1959.]

[4] Powell and Sheppard, *Spectrochim. Acta*, 1958, **13**, 69.
[5] Brown, Sheppard, and Simpson, *Discuss. Faraday Soc.*, 1950, **9**, 261.
[6] Bellanato, *Anales. Fis. Quim.*, 1956, **52**, *B*, 363.
[7] Chatt and Duncanson, *J.*, 1953, 2939.

---

622. *Lycopodium Alkaloids. Part I. Extraction of Alkaloids from* Lycopodium fawcettii, *Lloyd and Underwood.*[1]

By R. H. Burnell.

Plant material collected near Cinchona, in the Blue Mountain Range of Jamaica (*ca.* 5500 ft. elevation), was extracted by a procedure similar to that of Manske and Marion.[2] The crude ether-soluble base was separated into strong and weak bases by countercurrent distribution and the strong bases were distributed again. Although no separation of the stronger bases could be detected from the weight curve, the following compounds were isolated from fractions:

Base A, obtained as the perchlorate, $C_{16}H_{27}O_2N,HClO_4$, showed an infrared carbonyl peak at 1695 cm.$^{-1}$ as well as a bonded hydroxyl absorption at 3340 cm.$^{-1}$.

Base B, which melted at 178—179°, gave a perchlorate, m. p. 314—315°, identical (mixed m. p. and infrared comparison) with the *Lycopodium* alkaloid L.30 [3] described by

[1] Lloyd and Underwood, *Bull. Torrey Bot. Club.*, 1900, **27**, 167.
[2] Manske and Marion, *Canad. J. Res.*, 1946, **24**, *B*, 57.
[3] Perry and MacLean, *Canad. J. Chem.*, 1956, **34**, 1189.

Manske and Marion.[4] The base contained no *N*-methyl group and gave infrared maxima at 1703 and 3195 cm.$^{-1}$. Active-hydrogen determinations agree with an earlier suggestion that the nitrogen atom is tertiary.

Base C, the major component, was named fawcettiine and was characterised as its perchlorate, $C_{18}H_{29}O_3N,HClO_4,H_2O$ (m. p. 272—273°), which showed, besides hydroxyl peaks at 3463(H_2O) and 3229 cm.$^{-1}$, infrared absorption characteristic of an *O*-acetyl group (1732, 1250, and 1238 cm.$^{-1}$). Methoxyl and *N*-methyl groups are absent and the nitrogen is tertiary. The presence of the acetyl group has been confirmed by both analysis and hydrolysis of fawcettiine to deacetylfawcettiine, $C_{16}H_{27}O_2N$, which no longer absorbed in the carbonyl region. Active-hydrogen determinations indicate two hydroxyl groups to be present in deacetylfawcettiine and this confirms the molecular formula for fawcettiine which can therefore contain only one. Kuhn–Roth figures are inconclusive. Dehydration of deacetylfawcettiine with thionyl chloride afforded a new unsaturated compound, deacetyldehydrofawcettiine, characterised as the hygroscopic hydrochloride $C_{16}H_{25}ON,HCl$.

One further base (D) (10 mg.) was obtained from the distribution but this was identical with deacetylfawcettiine.

From the mixture of weak bases a small quantity of a crystalline perchlorate was obtained directly. The base, E, is $C_{17}H_{25}O_2N$ and shows a broad infrared carbonyl band (1697 cm.$^{-1}$); hydroxyl absorption is absent. A distinguishing feature of the infrared spectrum of Base E perchlorate is an ammonium band of medium intensity at 2020 cm.$^{-1}$ which is absent from the spectra of the salts of the other bases isolated.

From the remaining weak bases a volatile alkaloid was distilled. This is the second most abundant, and has been named fawcettidine (Base F). Analyses suggest $C_{16}H_{23}ON$ as the molecular formula and while the picrate is normal, the hydrochloride apparently decomposes during recrystallisation. The infrared carbonyl absorption of 1740 cm.$^{-1}$ must be due to a five-membered ring ketone. The base gives a dark orange colour with diazotised sulphanilic acid.

The residue from the distillation of fawcettidine afforded a perchlorate, m. p. 198°, $C_{18}H_{27}O_3N,HClO_4$ (Base G) which showed two infrared carbonyl peaks and a hydroxyl stretching band at 3450 cm.$^{-1}$.

To check the analyses of the alkaloids perchlorate determinations were carried out with essentially the method described by Bodenheimer and Weiler.[5] Results of reasonable accuracy could be obtained on samples containing as little as 1 mg. of perchlorate ion, but with smaller quantities discrepancies arose owing to discoloration of the reagent by the alkaloids.

Experimental.—Infrared spectra are for KBr pellets unless stated to the contrary.

Extraction. The dried ground plant material (16 kg.) was extracted continuously with methanol for 48 hr. and the solution concentrated to a thick black residue *in vacuo*. The residue was digested for 24 hr. with dilute hydrochloric acid. The solution was then filtered and neutral components were removed by ether-extraction. After basification with ammonia the crude ether-soluble base (19·0 g.) was obtained by continuous ether-extraction. Chloroform extraction of the aqueous layer afforded a further 9·5 g. of crude base, which is being studied.

Ether-soluble bases. The brown oil from the extraction (19·0 g.) was distributed between aqueous phosphate buffer (pH 5·28) and chloroform (stationary phase) in a 20-tube multiple extractor, a single-withdrawal technique being used until 34 transfers were complete. To the individual tubes was added concentrated aqueous ammonia (*ca.* 15 ml.), and the aqueous layer chloroform extracted three times. The extracts from each tube were combined and evaporated and then grouped as follows: Fraction A (weak bases), tubes 1—10 (8·7 g.); Fraction B (weak bases), tubes 11 – 18 (1·3 g.); Fraction C (strong bases), tubes 19—35 (6·6 g.).

Strong bases. Fraction C (6·5 g.) from the first distribution was shaken between chloroform (stationary phase) and acetate buffer (pH 5·23) for 20 transfers. The weight curve for the aqueous and organic phases showed no definite separation of the bases but the following products were obtained :

[4] Manske and Marion, *J. Amer. Chem. Soc.*, 1947, **69**, 2126.
[5] Bodenheimer and Weiler, *Analyt. Chem.*, 1955, **27**. 1293.

Base A. Fractions 3—7 (570 mg.) gave a crystalline *perchlorate* (270 mg.) which recrystallised from acetone and then water as colourless prisms, m. p. 221—222° (Found: C, 52·2; H, 7·3; N, 3·8. $C_{16}H_{27}O_2N,HClO_4$ requires C, 52·5; H, 7·7; N, 3·8%), infrared peaks at 1695 and 3340 cm.$^{-1}$.

Base B. Fractions 9—10 (860 mg.) gave a crystalline *base* (540 mg.) which recrystallised from acetone as plates, m. p. 178—179° (Found: C, 72·8; H, 9·3; O, 11·8; N, 5·1. $C_{16}H_{25}O_2N$ requires C, 73·0; H, 9·6; O, 12·2; N, 5·3%). Analyses for OCH_3 and *N*-CH_3 were nil. Active-hydrogen determination gave 0·27% at 21°; $C_{16}H_{24}ON(OH)$ requires 0·36%. Mixed m. p. with L.30 showed no depression. The base gave a crystalline *perchlorate*, rhombic plates, m. p. 314—315° (Found: N, 3·9; ClO_4^-, 27·6. $C_{16}H_{25}O_2N,HClO_4$ requires N, 3·9; ClO_4^-, 27·4%). The infrared spectrum (Nujol), which showed peaks at 1703 and 3195 cm.$^{-1}$, was identical to that of L.30 perchlorate.

Base C (Fawcettiine). Fractions 13—17 (2·52 g.) gave a crystalline *perchlorate* (1·7 g.), from acetone or water as prisms, m. p. 272—275° (decomp.) (Found: C, 50·7; H, 7·5; N, 3·3; ClO_4^-, 22·7; Cl, 8·5. $C_{18}H_{29}O_3N,HClO_4,H_2O$ requires C, 50·8; H, 7·6; N, 3·3; ClO_4^-, 23·3; Cl, 8·3%). Methoxyl groups were absent and analysis for *O*-Ac residues gave 9·2% (one acetyl group requires 10·1%).

The base regenerated from the perchlorate was a glass which sublimed with slight decomp. (100°/1 mm.) and readily decolorised a solution of potassium permanganate in acetone but did not react with bromine water, tetranitromethane, or potassium metaperiodate. The alkaloid is readily destroyed by nitric acid giving a highly insoluble brick-red amorphous substance, and the hydrobromide and hydrochloride decompose on recrystallisation.

The base was refluxed for 3 min. with excess of methyl iodide and then concentrated *in vacuo*, affording *fawcettiine methiodide* as a white solid, m. p. 279—280°, which was recrystallised from acetone (Found: C, 48·5; H, 7·1; N, 3·2; I, 28·2. $C_{19}H_{32}O_3NI,H_2O$ requires C, 48·8; H, 7·3; N, 3·0; I, 27·2%).

To fawcettiine (140 mg.) in methanol (10 ml.) was added 5N-sodium hydroxide in 50% methanol (7 ml.), and the solution kept at room temperature for 15 hr. Dilution with water and chloroform extraction gave white *deacetylfawcettiine* (110 mg.), m. p. 203—204° (needles from acetone) (Found: C, 72·1; H, 10·1; O, 12·2; N, 5·5. $C_{16}H_{27}O_2N$ requires C, 72·4; H, 10·3; O, 12·1; N, 5·3%). Active-hydrogen determination gave 0·413% at 21° and 0·303% at 90° (0·38% required for one mol.). The base showed no infrared carbonyl absorption. Acidification of an acetone solution of the base with perchloric acid diluted with acetone gave the *perchlorate*, m. p. 224—227° (Found: N, 3·9. $C_{16}H_{27}O_2N,HClO_4$ requires N, 3·8%).

Deacetylfawcettiine was dissolved in benzene and treated with excess of thionyl chloride at room temperature for 90 min. The residue after evaporation *in vacuo* was taken up in methanol containing a trace of hydrochloric acid and then evaporated to dryness. The white *deacetyldehydrofawcettiine hydrochloride* was recrystallised from methanol–acetone (Found: C, 67·2; H, 9·5; N, 4·9; Cl, 12·4. $C_{16}H_{25}ON,HCl$ requires C, 67·7; H, 9·3; N, 4·9; Cl, 12·5%).

Weak bases. Base E. Fraction A from the first distribution was taken up in acetone and made slightly acidic with perchloric acid. After several days a crystalline *perchlorate* (80 mg.), m. p. 267—269° (decomp.), was collected (Found: C, 55·0; H, 7·4; N, 3·8; Cl, 9·3. $C_{17}H_{25}O_2N,HClO_4$ requires C, 54·3; H, 7·0; N, 3·7; Cl, 9·4), infrared peak at 1697 cm.$^{-1}$.

Base F. The base regenerated from the mother liquors of Base E was distilled at 0·1 mm. giving a volatile colourless *oil* (780 mg.) at 125° (Found: C, 78·5; H, 9·4. $C_{16}H_{23}ON$ requires C, 78·3; H, 9·5%). Treatment with an ethereal solution of picric acid afforded the *picrate*, m. p. 222—223° (Found: C, 56·1; H, 5·5; N, 12·0; O, 26·5. $C_{16}H_{23}ON,C_6H_3O_7N_3$ requires C, 55·7; H, 5·5; N, 11·8; O, 26·2%). Both the base (liquid film) and the picrate (Nujol) showed an infrared carbonyl peak at 1740 cm.$^{-1}$.

Base G. The residue from the distillation was dissolved in dilute hydrochloric acid, filtered, and extracted with ether to remove neutral impurities. After basification with ammonia the crude base was extracted with ether and converted into the *perchlorate* (112 mg.), m. p. 198—200° (Found: C, 53·6; H, 7·3; N, 3·4; ClO_4^-, 25·2. $C_{18}H_{27}O_3N,HClO_4$ requires C, 53·3; H, 7·0; N, 3·4; ClO_4^-, 24·5%), infrared peaks at 3450, 1740, and 1694 cm.$^{-1}$.

The author thanks Dr. A. W. Sangster (U.C.W.I.) for the infrared spectra, Dr. A. R. Loveless (Dept. of Botany, U.C.W.I.) for identifying the *Lycopodium* and for his assistance in collecting the material, and Dr. L. Marion (N.R.C., Ottawa) for a sample of L.30.

University College of the West Indies,
Kingston 7, Jamaica.

[*Received, March 5th*, 1959.]

XUM

623. *Syntheses of the Four Dimethoxy-*N*-methylphthalimides.*

By H. R. Arthur and (Miss) Y. L. Ng.

In our work on the benzophenanthridine alkaloids, nitidine and oxynitidine,[1] we had occasion to prepare 4 : 5-dimethoxy-*N*-methylphthalimide which was shown to be a degradation product of oxynitidine. We also synthesised 3 : 4-dimethoxy-*N*-methylphthalimide which is a degradation product obtainable from chelerythrine.[2] Our syntheses of these two known compounds include variations in the methods previously used.

The two remaining previously unknown dimethoxy-*N*-methylphthalimides have also been synthesised. Ultraviolet spectra are recorded.

Experimental.—Except where otherwise stated m. p.s (which are uncorrected) were taken with a gas-heated copper block.

3 : 4-*Dimethoxy-N-methylphthalimide*. *o*-Vanillin (30·0 g.) was melted and potassium hydroxide (16 g.) in water (24 ml.) was added, with stirring, at a rate of 2 drops per second. Purified methyl sulphate (24 ml.) was then added at the same rate. After 2 hr. ice was added. The precipitate of crude *o*-veratraldehyde (30·0 g.) was collected, washed with ice-water, and dried. This product (10·0 g.) was oxidised by the method of Edwards, Perkin, and Stoyle [3] to *o*-veratric acid (10·0 g.), m. p. 120°, which was converted into crude meconine (5·0 g.), m. p. 100°. This product (3·0 g.), with manganese dioxide, yielded opianic acid (3·0 g.), m. p. 145°, which with lead dioxide gave hemipinic acid [3] (1·0 g.), m. p. 173—175° (after drying at 120°). Anhydrous hemipinic acid (0·5 g.) was heated with acetyl chloride (10 ml.) for 1 hr. Distillation of the halide left a residue which was dissolved in glacial acetic acid. Sodium acetate (1·0 g.) and methylamine hydrochloride (0·8 g.) were added and the mixture was heated under reflux for 20 min., after which removal of inorganic salts and concentration of the filtrate gave a product which was dissolved in benzene. The benzene solution was filtered through alumina and then concentrated. Colourless needles of 3 : 4-dimethoxy-*N*-methylphthalimide (0·08 g.), m. p. 166—167°, were obtained (Found: C, 60·2; H, 5·1; N, 6·6; OMe, 27·8%; *M*, 215. Calc. for $C_{11}H_{11}O_4N$: C, 59·7; H, 5·0; N, 6·3; 2OMe, 28·0%; *M*, 221), $\lambda_{max.}$ (log ε), 337 (3·71), 234 mμ (2·53).

3 : 5-*Dimethoxy-N-methylphthalimide*. Benzoic acid (10 g.) was heated under reflux with fuming sulphuric acid (65% SO_3; 24 ml.) for 10 hr. at 160—175°, then for 5 hr. at 180—190°. The cooled mixture was added slowly to a suspension of barium carbonate (300 g.) in water (1 l.). The mixture was boiled, then filtered hot; the residue was washed with hot water. The combined filtrates were treated with a concentrated solution of potassium carbonate until precipitation of barium carbonate was just complete. The precipitate was removed, and the filtrate, after concentration under reduced pressure, deposited the potassium salt of 3 : 5-disulphobenzoic acid (35·0 g.). Fusion of this salt (30·0 g.) with potassium hydroxide (70 g.), suspended in water (15 ml.), by Birkinshaw and Bracken's method [4] yielded 3 : 5-dihydroxybenzoic acid (5·0 g.), m. p. 234°, which gave a port-wine colour with ferric chloride solution. This product (10·0 g.) was converted into 3 : 5-dimethoxybenzoic acid (9·8 g.), m. p. 182—184°, by methyl sulphate. To 3 : 5-dimethoxybenzoic acid (10·0 g.) in absolute ethanol (30 ml.) was added concentrated sulphuric acid (2·5 ml.) with shaking. The mixture was boiled under reflux for 6 hr., and the product, isolated in the usual manner, was treated with a mixture of concentrated sulphuric acid (35 ml.), water (7 ml.), and chloral hydrate (12·0 g.) as stated by Graves and Adams.[5] 4 : 6-Dimethoxy-3-(trichloromethyl)phthalide (18·0 g.), m. p. 245—248° (lit., m. p. 125°), was obtained. This was converted into 4 : 6-dimethoxyphthalide-3-carboxylic acid (7·7 g.), which (2·0 g.) was decarboxylated and then oxidised [5] with potassium permanganate to give 3 : 5-dimethoxyphthalic acid (1·0 g.), m. p. 155—158° (decomp.). This acid (1·0 g.) was boiled under reflux with acetic anhydride (20 ml.) for 2 hr. The solvent was distilled, then glacial acetic acid, fused sodium acetate (3·0 g.), and methylamine hydrochloride (2·0 g.) were added and the mixture was treated as stated for the preparation above. 3 : 5-*Dimethoxy-N-methylphthalimide* (0·15 g.) was obtained as colourless prisms, m. p. 185° (m. p. 195°; Kofler) (Found; C, 59·9; H, 5·2; N, 6·5; OMe, 27·9%; *M*, 234), $\lambda_{max.}$ (log ε) 342 (3·63), 239 mμ (4·50).

[1] Arthur, Hui, and Ng, *J.*, 1959, 1840.
[2] Späth and Kuffner, *Ber.*, 1931, **64**, 1123.
[3] Edwards, Perkin, and Stoyle, *J.*, 1925, 195.
[4] Birkinshaw and Bracken, *J.*, 1942, 369.
[5] Graves and Adams, *J. Amer. Chem. Soc.*, 1923, **45**, 2439.

3 : 6-*Dimethoxy*-N-*methylphthalimide*. *p*-Benzoquinone (purification was essential; 1·0 g.) was converted by Helferich's method [6] into 2 : 3-dicyanoquinol, obtained as brown hydrated crystals (0·5 g.) which blackened at 230°. This product (0·5 g.) was converted by Thiele and Meisenheimer's method [7] into 3 : 6-dihydroxyphthalimide (0·55 g.), which separated from water as greenish-yellow needles. 3 : 6-Dihydroxyphthalimide (0·25 g.) was ground with potassium carbonate (1·0 g.). The bright red potassium salt obtained was heated in a sealed tube with methyl iodide (4 ml.) on a steam-bath. After 4 hr. the mixture changed from red to brown. After 8 hr. the methyl iodide was evaporated and the residue was washed with water, then recrystallised from alcohol. Buff-coloured needles (0·1 g.) of 3 : 6-*dimethoxy*-N-*methylphthalimide*, m. p. 202—204° (m. p. 206—208°; Kofler), separated (Found: C, 60·2; H, 5·2; N, 7·0; OMe, 27·7%; *M*, 235), $\lambda_{max.}$ (in ethanol) 221 mμ (log ε 4·27) [between 285 and 310 mμ the extinction coefficient remained approximately constant (log ε 2·6)].

4 : 5-*Dimethoxy*-N-*methylphthalimide*. By the method of Edwards, Perkin, and Stoyle,[3] veratraldehyde was converted into veratric acid, m. p. 175°. The acid (10·0 g.) was converted into *m*-meconine, colourless needles (3·2 g.), m. p. 153—156°. This (1·0 g.) with potassium permanganate gave yellow *m*-hemipinic acid (0·5 g.), m. p. 193—199° (decomp.), which (0·5 g.) was converted into the anhydride and into 4 : 5-dimethoxy-*N*-methylphthalimide (0·1 g.), as stated in an earlier communication.[1] The product crystallised from alcohol as colourless prisms, m. p. 256—258° (214—225° decomp.; Kofler), $\lambda_{max.}$ (log ε), (in ethanol), 295 (3·24), 247 mμ (4·69). Deulofeu *et al.*[8] give $\lambda_{max.}$ (log ε) 295 (3·22), 261 mμ (3·73).

The authors thank Professor J. E. Driver for his interest and gratefully acknowledge financial support from the Research Grants Committee of the University of Hong Kong.

UNIVERSITY OF HONG KONG, HONG KONG. [*Received, March 23rd*, 1959.]

[6] Helferich, *Ber.*, 1921, **54**, 157; Helferich and Bodenbender, 1923, **56**, 1113.
[7] Thiele and Meisenheimer, *Ber.*, 1900, **33**, 676.
[8] Vernengo, Cerezo, Iaccobucci, and Deulofeu, *Annalen*, 1957, **610**, 173.

624. *Carcinogenic Nitrogen Compounds. Part XXVII.*[1] *Benzacridines and Related Compounds Derived from* o-*Ethylaniline.*

By NG. PH. BUU-HOÏ and P. JACQUIGNON.

IN a broad investigation on the relation between structure and carcinogenic activity of angular benzacridines,[2] it was of interest to determine the influence of a 9-ethyl group in the 1,2- and 3,4-benzacridine series; in the corresponding homocyclic group, 5-ethyl-1,2-benzanthracene has considerable activity.[3]

In the 1,2-benzacridine series, condensation of *o*-ethylaniline with α-naphthol in the presence of iodine [4] furnished *N*-*o*-ethylphenyl-1-naphthylamine, and Bernthsen reactions of this secondary amine with acetic anhydride and higher homologues afforded the 5-alkyl-9-ethyl-1,2-benzacridines listed in Table 1; 9-ethyl-1,2-benzacridine was prepared directly from *o*-ethylaniline with α-naphthol and paraformaldehyde.[5] A similar reaction with β-naphthol yielded 9-ethyl-3,4-benzacridine, and several of its 5-alkyl derivatives, obtained by Bernthsen reactions with *N*-*o*-ethylphenyl-2-naphthylamine, are listed in Table 2.

TABLE 1. 9-*Ethyl*-1,2-*benzacridines* (I).

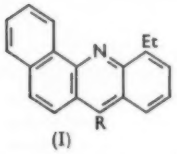
			Found (%)			Reqd. (%)		
Substituent	M. p.	Formula	C	H	N	C	H	N
H	127°	$C_{19}H_{15}N$	88·4	6·1	5·1	88·7	5·9	5·4
Me	115	$C_{20}H_{17}N$	88·2	6·0	—	88·5	6·3	—
picrate	157	$C_{26}H_{20}O_7N_4$	—	—	10·8	—	—	11·2
Et	94	$C_{21}H_{19}N$	88·3	6·6	4·7	88·4	6·7	4·9
picrate	135	$C_{27}H_{22}O_7N_4$	—	—	10·6	—	—	10·9
Pr	77	$C_{22}H_{21}N$	88·1	6·9	—	88·3	7·1	—

[1] Part XXVI, Buu-Hoï, Saint-Ruf, Jacquignon, and Barrett, *J.*, 1958, 4308.
[2] Cf. Lacassagne, Buu-Hoï, Daudel, and Zajdela, *Adv. Cancer Res.*, 1956, **4**, 315.
[3] Cook, Robinson, and Goulden, *J.*, 1936, 393.
[4] Knoevenagel, *J. prakt. Chem.*, 1914, **89**, 1; Buu-Hoï, *J.*, 1952, 4346.
[5] Ullmann and Fetvadjian, *Ber.*, 1903, **36**, 1027; Buu-Hoï, *J.*, 1949, 670.

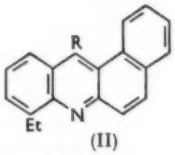
XUM

TABLE 2. *9-Ethyl-3,4-benzacridines* (II).

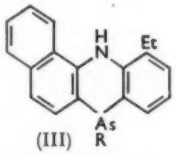
Substituent	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Reqd. (%) C	Reqd. (%) H	Reqd. (%) N
H	106°	$C_{19}H_{15}N$	88·4	6·0	5·3	88·7	5·9	5·4
picrate	275	$C_{25}H_{18}O_7N_4$	—	—	11·4	—	—	11·5
Me	72	$C_{20}H_{17}N$	88·2	6·3	—	88·5	6·3	—
picrate	238	$C_{26}H_{20}O_7N_4$	—	—	10·9	—	—	11·2
Et	110	$C_{21}H_{19}N$	88·7	6·8	4·6	88·4	6·7	4·9
picrate	220	$C_{27}H_{22}O_7N_4$	—	—	10·7	—	—	10·9
Pr	76	$C_{22}H_{21}N$	88·0	6·8	—	88·3	7·1	—



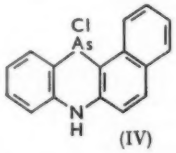
(I)



(II)

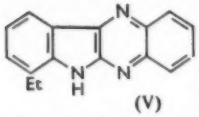


(III)



(IV)

Condensation of *N-o*-ethylphenyl-1- and -2-naphthylamine with arsenic trichloride [6] readily afforded 10-chloro-6-ethyl-5,10-dihydro-3,4-(III; R = Cl) and -1,2-benzophenarsazine (IV); Grignard reaction of the former with methylmagnesium iodide gave 6-ethyl-5,10-dihydro-10-methyl-3,4-benzophenarsazine (III; R = Me).



(V)

Other nitrogen-heterocyclic compounds prepared from *o*-ethylaniline include 8-ethyl-2,4-dimethylquinoline, obtained by a Combes reaction with acetylacetone,[7] and 7-ethylisatin, which was readily prepared by the Sandmeyer reaction [8] although other *o*-substituted anilines resist conversion into isatins by this method.[9] Condensation of 7-ethylisatin with *o*-phenylenediamine yielded the indophenazine (V).

The biological properties of these compounds are being investigated; preliminary results show 9-ethyl-5-methyl-1,2-benzacridine to be carcinogenic.

Experimental (with R. ROY).—*o*-Ethylaniline was prepared by reduction of *o*-ethylnitrobenzene; its *toluene*-p-*sulphonyl derivative* crystallised as prisms, m. p. 135°, from ethanol (Found: C, 65·2; H, 6·4. $C_{15}H_{17}O_2NS$ requires C, 65·4; H, 6·1%).

1-*o*-*Ethylphenyl*-2,5-*dimethylpyrrole*. A mixture of hexane-2,5-dione (5 g.) and *o*-ethylaniline (6·5 g.) was refluxed with acetic acid (1 drop) until water ceased to be evolved, and the product was fractionated *in vacuo*, giving the *pyrrole* (5 g.), b. p. 138°/15 mm. (Found: C, 84·1; H, 8·5; N, 6·7. $C_{14}H_{17}N$ requires C, 84·4; H, 8·6; N, 7·0%).

N-*o*-*Ethylphenyl*-1-*naphthylamine*. *o*-Ethylaniline (150 g.), α-naphthol (190 g.), and iodine (0·5 g.) were refluxed for 24 hr., and the product fractionated *in vacuo*, giving the *amine* (62 g.), b. p. 233°/11 mm. (Found: C, 87·3; H, 6·9. $C_{18}H_{17}N$ requires C, 87·4; H, 6·9%). The isomeric N-*o*-*ethylphenyl*-2-*naphthylamine*, similarly prepared from β-naphthol, had b. p. 240°/14 mm. (Found: C, 87·2; H, 7·0%).

Preparation of the benzacridines (see Tables). Those not substituted in the 5-position were prepared by addition of paraformaldehyde (5 g.) in small portions to a boiling mixture of *o*-ethylaniline (10 g.) and α- or β-naphthol (15 g.), and fractionation of the product *in vacuo*. The portion of b. p. 265—275°/15 mm. was dissolved in ethanol and treated with picric acid; the picrate was precipitated on cooling and recrystallised from ethanol; the free benzacridine obtained on basification with aqueous ammonia was recrystallised from ethanol (yield, 15—35%). The 5-alkylated benzacridines were prepared by refluxing for 24 hr. a mixture of the secondary arylamine with an excess of the appropriate acid anhydride and fused zinc chloride; after cooling, the dark mass was treated with aqueous sodium hydroxide and the product was taken up in benzene and fractionated *in vacuo*, purification being *via* the picrate as above (yield, 30—45%).

10-*Chloro*-6-*ethyl*-5,10-*dihydro*-3,4-*benzophenarsazine* (III; R = Cl). A solution of *N-o*-ethylphenyl-1-naphthylamine (3 g.) and arsenic trichloride (2·2 g.) in *o*-dichlorobenzene (5 c.c.)

[6] Cf. Lewis and Hamilton, *J. Amer. Chem. Soc.*, 1921, **43**, 2219; Burton and Gibson, *J.*, 1926, 2243; Buu-Hoï and Royer, *J.*, 1951, 795.

[7] Combes, *Compt. rend.*, 1888, **106**, 1536; Buu-Hoï and Guettier, *Rec. Trav. chim.*, 1946, **65**, 502.

[8] Sandmeyer, *Helv. Chim. Acta*, 1919, **2**, 234.

[9] Cf. Yen, Buu-Hoï, and Xuong, *J. Org. Chem.*, 1958, **23**, 1858.

was gently refluxed for 1 hr.; the *phenarsazine* (4 g.) formed on cooling and addition of cyclohexane was recrystallised from toluene as golden-yellow needles, m. p. 211°, giving a blood red halochromy in sulphuric acid (Found: C, 61·0; H, 4·2. $C_{18}H_{15}NAsCl$ requires C, 60·8; H, 4·2%).

6-*Ethyl*-5,10-*dihydro*-10-*methyl*-3,4-*benzophenarsazine* (III; R = Me) was prepared by refluxing the foregoing phenarsazine (0·2 g.) with ethereal Grignard reagent from methyl iodide (0·5 g.) and magnesium for 20 min. on a water-bath; after decomposition with aqueous ammonium chloride and evaporation of the solvent, the precipitate obtained (0·15 g.) was recrystallised from methanol as needles, m. p. 96°, giving an orange-yellow halochromy in sulphuric acid (Found: C, 67·7; H, 5·1. $C_{19}H_{18}NAs$ requires C, 68·0; H, 5·4%).

10-*Chloro*-6-*ethyl*-5,10-*dihydro*-1,2-*benzophenarsazine* (IV). Prepared from *N*-*o*-ethylphenyl-2-naphthylamine (3 g.) and arsenic trichloride (22 g.) in the usual way, this *compound* crystallised as golden-yellow needles, m. p. 225°, from toluene, giving an orange-red halochromy in sulphuric acid (Found: C, 60·5; H, 4·3%).

8-*Ethyl*-2,4-*dimethylquinoline*. A mixture of acetylacetone (10 g.) and *o*-ethylaniline (12 g.) was refluxed for 1 hr., and, after cooling, treated with warm sulphuric acid (80 c.c.); the product obtained on basification with cold aqueous ammonia was taken up in benzene, the benzene solution washed with water and dried (Na_2SO_4), the solvent distilled off, and the residue fractionated *in vacuo*. The *quinoline* (8 g.) had b. p. 148°/13 mm., n_D^{22} 1·5988, and crystallised in the refrigerator (Found: C, 84·2; H, 8·3. $C_{13}H_{15}N$ requires C, 84·3; H, 8·2%). The *picrate* formed yellow leaflets, m. p. 168—169°, from ethanol (Found: N, 13·5. $C_{19}H_{18}O_7N_4$ requires N, 13·5%).

7-*Ethylisatin*. A solution of *o*-ethylaniline hydrochloride (7 g.), chloral hydrate (9 g.), hydroxylamine hydrochloride (11 g.), and sodium sulphate (130 g.) was heated to the b. p. during 45 min. and kept at that temperature for 2 min.; the aqueous phase was then decanted and the solid residue washed with water and heated with sulphuric acid (50 c.c.) for 10 min. at 70—80°. The *product* was then poured on ice, and the solid precipitate washed with water and recrystallised from ethanol, giving orange needles, m. p. 193° (Found: C, 68·3; H, 5·1; N, 8·3. $C_{10}H_9O_2N$ requires C, 68·6; H, 5·1; N, 8·0%).

7-*Ethylindophenazine* (V). A solution of 7-ethylisatin (1 g.) and *o*-phenylenediamine (0·7 g.) in acetic acid (10 c.c.) was refluxed for 20 min., and the precipitate (1·2 g.) obtained on dilution with water formed yellow leaflets, m. p. 268°, from ethanol, giving a brown halochromy in sulphuric acid (Found: N, 16·8. $C_{16}H_{13}N_3$ requires N, 17·0%). 7-*Ethyl*-2- or -3-*nitroindophenazine*, similarly prepared with 4-nitro-1,2-phenylenediamine, crystallised as orange, sublimable needles, m. p. 263°, from acetic acid (Found: N, 18·9. $C_{16}H_{12}O_2N_4$ requires N, 19·2%).

This investigation was supported in part by a research grant from the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service; the authors thank the authorities concerned.

THE RADIUM INSTITUTE, THE UNIVERSITY OF PARIS. [*Received, March 25th*, 1959.]

625. *Molybdenum*(II) *Benzoate*.

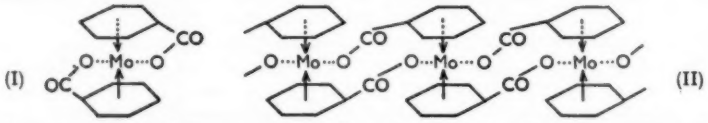
By E. W. ABEL, APAR SINGH, and G. WILKINSON.

RECENTLY a number of workers have reported [1-4] the reaction between substituted aromatic compounds and chromium hexacarbonyl to produce tricarbonyl aromatic chromium compounds. It has been noted,[1] however, that certain substituents (CO_2H, CN, CHO, NO_2) on the aromatic nucleus cause decomposition, with no formation of a metal-tricarbonyl compound.

In the process of treating molybdenum hexacarbonyl with a variety of compounds, we have obtained molybdenum dibenzoate, $(C_6H_5{\cdot}CO_2)_2Mo$, by the direct interaction of benzoic acid and the hexacarbonyl in dimethylcarbitol (diethylene glycol dimethyl ether). This compound we believe is a novel type of oxygen chelate complex, (I) and (II), where,

[1] Nicholls and Whiting, *J.*, 1959, 551.
[2] Natta, Ercoli, and Calderazzo, *Chim. e Ind.*, 1958, **40**, 287.
[3] Fischer, Öfele, Essler, Frohlich, Mortensen, and Semmlinger, *Z. Naturforsch.*, 1958, **13**b, 458.
[4] Fischer and Öfele, *Chem. Ber.*, 1957, **90**, 2532.

in addition, the arene nucleus is bound to the metal atom by a sandwich-type bond, as in the arene–metal carbonyls.



The absence of the CO_2H group is confirmed by the insolubility of the substance in alkali, and the failure to liberate any hydrogen chloride on warming with either phosphorus pentachloride or thionyl chloride. Further, there are no hydroxyl frequencies observable in the infrared spectrum, either in the free OH or hydrogen-bonded OH regions.

There is also a complete absence of absorption in the metal carbonyl and carboxylic acid regions, but the presence of the $-C\begin{matrix}O^-\\O\end{matrix}$ group is confirmed by very strong absorption at 1404 and 1494 cm.$^{-1}$, these two regions being very characteristic [5] of the symmetrical and asymmetrical vibrations of the COO^- structure.

From the structures proposed it can be seen that it is possible for the aromatic ring to co-ordinate to the same (I) or different (II) metal atoms from its carboxylate group, the latter giving chain formation. This polymerisation is confirmed by the solubility properties of the compound. A very small portion of the initial product is soluble in chloroform to give a bright yellow solution which undergoes rapid decomposition; the residual yellow crystals, however, are completely insoluble in any solvent. These possess remarkable thermal stability and have been recovered unchanged after 24 hours' heating at 350° in the absence of air.

The polymeric structure does break down at a higher temperature, however, and it is possible to sublime molybdenum dibenzoate at 420°/0·01 mm. The crystalline yellow condensate has identical analysis and infrared spectrum with those of an unsublimed sample. Again, the condensed compound appears to be mainly polymeric and has the same solubility properties as it had before sublimation.

Similar compounds with the same properties have also been obtained from *o*-toluic and anisic acids. These also have very strong infrared absorptions in the COO^- regions, *viz.*: molybdenum *o*-toluate (1384 and 1500 cm.$^{-1}$), and molybdenum anisate (1390 and 1504 cm.$^{-1}$). All three compounds were diamagnetic. The reaction of nitrobenzene with molybdenum hexacarbonyl gives a blue, insoluble, presumably polymeric material, perhaps of a rather similar nature to the benzoate; we have been unable to purify the material or to obtain reliable analyses.

Experimental.—Microanalyses were by the Microanalytical Laboratory, Imperial College. Infrared spectra, in Nujol and hexachlorobutadiene mulls and potassium bromide discs, were recorded on a Perkin-Elmer Model 21 double-beam spectrometer with sodium chloride optics.

Interaction of molybdenum hexacarbonyl and benzoic acid. The carbonyl (5·0 g., 1 mol.) and acid (4·7 g., 2 mol.) in freshly distilled diethylene glycol dimethyl ether were heated at 160° until there was no further evolution of carbon monoxide (about 9 hr.). Crystals separated during the reaction, and after cooling, volatile matter was removed (60°/10^{-3} mm.). Washing with warm alcohol (4 × 20 c.c.) and subsequent vacuum drying left a mass of lemon-yellow needle crystals of *molybdenum*(II) *dibenzoate* (2·72 g., 38%) (Found: C, 49·7; H, 3·1; Mo, 28·0; O, 19·2. $C_{14}H_{10}O_4Mo$ requires C, 49·7; H, 3·0; Mo, 28·4; O, 18·9%).

In a similar manner *molybdenum di-o-toluate* (41%) (Found: C, 52·7; H, 4·5; Mo, 26·2; O, 17·4. $C_{16}H_{14}O_4Mo$ requires C, 52·5; H, 3·8; Mo, 26·2; O, 17·5%) and *molybdenum dianisate* (38%) (Found: C, 48·1; H, 4·3; Mo, 24·3; O, 23·7. $C_{16}H_{14}O_6Mo$ requires C, 48·2; H, 3·5; Mo, 24·1; O, 24·1%) were prepared as yellow crystalline solids.

Sublimation of molybdenum benzoate. The salt was placed under a thick pad of glass-wool in a small sublimer with an air-cooled probe. After evacuation (0·01 mm.), the sublimer was slowly heated in a Woods-metal bath. At *ca.* 350° the pale yellow crystals became orange (but returned to yellow on cooling), and then at *ca.* 420° yellow crystals started to condense on the

[5] Duval, Gerding, and Lecomte, *Rec. Trav. chim.*, 1950, **69**, 391 (and references listed therein).

probe. The temperature was kept at this value until most of the benzoate had sublimed. On cooling, the probe was removed and the condensate (78%) was unchanged molybdenum (II) benzoate (Found: C, 49·6; H, 3·05; Mo, 28·2; O, 19·0%) (strong infrared absorptions at 1404 and 1494 cm.$^{-1}$).

Infrared spectrum of molybdenum(II) *dibenzoate.* 677(s), 707(s), 717(s), 842(m), 930(w), 1028(m), 1067(w), 1137(m), 1172(w), 1404(vs), 1442(m), 1494(vs), 1583(m), 3020(w).

We thank the Climax Molybdenum Company for a gift of molybdenum hexacarbonyl and the Ethyl Corporation for financial support (E. W. A.).

INORGANIC CHEMISTRY RESEARCH LABORATORIES,
IMPERIAL COLLEGE, LONDON, S.W.7.

[*Received, March 26th*, 1959.]

626. *Iodyl Fluoride.*

By E. E. AYNSLEY and S. SAMPATH.

CHLORYL FLUORIDE, ClO_2F, has been shown by Woolf [1] and by Schmeisser and Ebonhöch [2] to form complex compounds with a number of inorganic fluorides including BF_3, SiF_4, AsF_5, SbF_5, and PF_5. The isolation by Schmeisser and Lang [3] of a white crystalline compound, IO_2F,AsF_5, from IO_2F and AsF_5 with use of anhydrous hydrogen fluoride suggested that other complexes of iodyl fluoride might be prepared. The similarity in the modes of decomposition of KIF_6 and IOF_3 led Aynsley, Nichols, and Robinson [4] to believe that IOF_3 might have the structure, $IO_2^+IF_6^-$ which suggests that IO_2F,AsF_5 should be written $IO_2^+AsF_6^-$. The reactions of iodyl fluoride have therefore been studied and attempts made to prepare complexes containing the IO_2^+ ion. The absence of results suggest that the arsenic complex may rather be formulated as $AsF_4^+IO_2F_2^-$, in view of the isolation of $K^+IO_2F_2^-$ by Helmholtz and Rogers.[5]

Iodyl fluoride dissolved readily in warm selenium tetrafluoride to form a clear liquid. The products were selenium oxyfluoride and iodine pentafluoride in amounts indicating that the reaction may be represented:

$$2SeF_4 + IO_2F = 2SeOF_2 + IF_5$$

Similarly, bromine trifluoride reacted vigorously with iodyl fluoride, producing iodine pentafluoride, oxygen, and bromine. One mole of oxygen was evolved for every mole of iodyl fluoride, probably in accordance with the equation:

$$3IO_2F + 4BrF_3 = 3IF_5 + 2Br_2 + 3O_2$$

Antimony pentafluoride when heated with iodyl fluoride forms a blue solid having the composition $IO_2F,0{\cdot}8SbF_5$.

On the other hand, boron trifluoride, silicon tetrachloride, arsenic pentafluoride, and sulphur trioxide when separately passed over iodyl fluoride at various temperatures did not react with it. Moreover, when boron trifluoride was passed into (*a*) a suspension of iodyl fluoride in " Arcton 9," (*b*) a solution of iodyl fluoride in iodine pentafluoride (cf. the reaction $KF + BF_3 = KBF_4$), and (*c*) iodyl fluoride dissolved in anhydrous hydrogen fluoride, no reaction occurred. Nor was there any reaction with nitryl fluoride, though a compound of the type $NO_2^+IO_2F_2^-$ might have been expected.

Thus iodyl fluoride is much less prone to form complex compounds than chloryl fluoride; some fluorinating agents, however, *e.g.*, SeF_4, BrF_3, convert iodyl fluoride into iodine pentafluoride.

The authors thank Imperial Chemical Industries Limited for the loan of a fluorine generator, and one of them (S. S.) is indebted to the U.K. Government for a maintenance grant under the Colombo Plan.

KING'S COLLEGE, NEWCASTLE UPON TYNE, 1.

[*Received, March 30th*, 1959.]

[1] Woolf, *J.*, 1954, 4113.
[2] Schmeisser and Ebonhöch, *Angew Chem.*, 1954, **66**, 230.
[3] Schmeisser and Lang, *ibid.*, 1955, **67**, 156.
[4] Aynsley, Nichols, and Robinson, *J.*, 1953, 623.
[5] Helmholtz and Rogers, *J. Amer. Chem. Soc.*, 1940, **62**, 1537.

627. *Some Fatty Acid Esters of α-Tocopherol.*

By P. F. G. Praill.

In view of the importance of some of the unsaturated fatty acids in the diet and the prevention of their autoxidation by the tocopherols it seemed that the biological study of the esters of α-tocopherol might be of interest. However, the fact that in autoxidative control the essential agent is free tocopherol was borne in mind. Several esters of α-tocopherol are well known but those of the fatty acids are restricted to the D- and the DL-forms of the acetate [1] and palmitate.[2] The present communication is to record the general characteristics of some other fatty acid esters.

Experimental.—Materials. Fatty acids were purified by standard procedures, and had m. p., n_D, and iodine value in good agreement with those reported in the literature. Acid chlorides were prepared by treatment with oxalyl chloride.

D-α-Tocopherol was a 70% concentrate or was prepared by hydrolysis of the pure acetate. DL-α-Tocopherol was a commercial sample (>99·5% pure).

Preparation of the esters of tocopherol. α-Tocopherol (0·02 mole) was dissolved in 1,2-dichloroethane (22·5 ml.) and pyridine (12·2 ml.). The acid chloride (0·022 mole) in 1,2-dichloroethane (17 ml.) was then added during 15 min., there being a transient pink coloration and pyridine hydrochloride separating. After 20 hr. at room temperature the mixture was poured into water and extracted with ether. The ethereal solution was washed with 2N-hydrochloric acid, then with 2% potassium hydroxide solution, and finally with water. The dried (Na_2SO_4) ethereal solution was evaporated, and the residue dissolved in the minimum amount of hot propan-2-ol. The oil, or solid, which separated from the propanol on cooling, was taken up in hot acetone. The treatment with alcohol and acetone was repeated until no further improvement in the spectrum of a sample was obtained.

The method for removing traces of acid from the esters used by Robeson *et al.*[2] was to adsorb the crude material from a light petroleum solution on " Doucil " and to re-extract the ester with large volumes of light petroleum. We tried this process using " Doucil " and also " Decalso F; " although some improvement of the crude materials was effected, generally the purification was not so good as by successive acetone extractions.

For the unsaturated esters the entire process was carried out in an inert atmosphere so far as possible.

Table 1. D-α-*Tocopheryl esters.*

Ester	M. p.	n_D^{20}	n_D^{50}	$E^{1\%}_{1\,cm.}$ *	log $\varepsilon_{max.}$ †	$E^{1\%}_{1\,cm.}$ ‡	log $\varepsilon_{max.}$ ¶	$[\alpha]_{5461}$ ¶	Yield (%)
Acetate [1]	26·5—27·5°	—	—	41·2	3·29	—	—	—	—
Acetate	—	1·4970	1·4860	—	—	46·5	3·34	+2·56°	—
Palmitate [2]	42—43	—	—	26·8	3·25	—	—	—	33
Palmitate [a,c] ...	42—43	—	—	—	—	27·9	3·27	—	50
Palmitate [b,d] ...	42	—	1·4792	31·0	3·32	31·7	3·33	+2·47	67
Stearate [e]	48·5	—	1·4782	—	—	30·5	3·33	+2·87	90
Oleate [a,f]	—	1·4960	1·4875	—	—	25·4	3·25	+2·44	32
Elaidate [g]	27·5	—	1·4814	—	—	32·0	3·35	+2·71	71
Petroselinate [h]	—	1·4928	1·4830	—	—	31·3	3·34	+2·86	42
Erucate [a,i]	−6 to −4	1·4946	1·4848	—	—	26·6	3·30	—	46
Brassidate [a,j] ...	35·2	—	1·4802	22·5	3·23	—	—	—	61
Linoleate [k]	—	1·4962	1·4888	—	—	33·1	3·36	+2·61	33
Linolenate [l] ...	—	1·5007	—	—	—	34·1	3·37	—	45

[a] From 70% tocopherol. [b] From pure tocopherol. [c] Found: C, 81·4; H, 11·6. $C_{45}H_{80}O_3$ requires C, 80·8; H, 12·0%. [d] Found: C, 80·6; H, 11·8%. [e] Found: C, 81·0; H, 11·9. $C_{47}H_{84}O_3$ requires C, 81·0; H, 12·1%. [f] Found: C, 81·3; H, 11·9%. $C_{47}H_{82}O_3$ requires C, 81·3; H, 11·7%. [g] Found: C, 81·4; H, 12·1%. [h] Found: C, 81·5; H, 11·7%. [i] Found: C, 81·3; H, 11·7. $C_{51}H_{90}O_3$ requires C, 81·6; H, 12·0%. [j] Found: C, 81·3; H, 11·7%. [k] Found: C, 81·6; H, 11·8. $C_{47}H_{80}O_3$ requires C, 81·5; H, 11·6%. [l] Found: C, 82·5; H, 11·2. $C_{47}H_{78}O_3$ requires C, 81·7; H, 11·3%.

* At 286 mμ in EtOH. † In EtOH. ‡ At 285 mμ in cyclohexane. ¶ In cyclohexane.

Table 1 gives the main characteristics of the D-α-tocopheryl esters, and Table 2 those for the DL-esters. Some values from the literature are included.

In cyclohexane, maximum absorption occurred at 285 mμ; there was a peak with an intensity approaching that of the maximum at 288 mμ, and a less intense peak at 279 mμ. Pure esters had little or no absorption at 300 mμ but partly isomerised materials had a low, but

[1] Robeson, *J. Amer. Chem. Soc.*, 1942, **64**, 1487.
[2] Baxter, Robeson, Taylor, and Lehman, *ibid.*, 1943, **65**, 918.

TABLE 2. DL-α-*Tocopheryl esters.*

Ester	M. p.	n_D^{20}	n_D^{50}	$E^{1\%}_{1\,cm.}$ *	log $\varepsilon_{max.}$ *	$E^{1\%}_{1\,cm.}$ ‡	log $\varepsilon_{max.}$ ¶	Yield (%)
Acetate [a]	—	1·4964	1·4860	44·4	3·32	45·4	3·33	—
Palmitate [b]	36—38°	—	—	30·9	3·31	—	—	—
Stearate [c]	40·5	—	1·4760	—	—	30·7	3·33	71
Oleate [d]	—	1·4918	—	—	—	32·0	3·35	48
Erucate [e]	—	1·4898	1·4800	27·3	3·31	—	—	42
Brassidate [f]	26·5	—	1·4800	28·7	3·33	—	—	82
Linoleate [g]	—	1·4960	—	—	—	35·4	3·39	48

[a] Material from Roche Products Ltd. [b] Ref. 2. [c] Found: C, 81·3; H, 12·2. $C_{47}H_{84}O_3$ requires C, 81·0; H, 12·1%. [d] Found: C, 81·3; H, 11·9. $C_{47}H_{82}O_3$ requires C, 81·3; H, 11·7%. [e] Found: C, 81·3; H, 11·7. $C_{51}H_{90}O_3$ requires C, 81·6; H, 12·0%. [f] Found: C, 81·9; H, 11·6. [g] From α-linoleic acid. Found: C, 81·2; H, 11·5. $C_{47}H_{80}O_3$ requires C, 81·5; H, 11·6%. *†‡¶ See Table 1.

measurable, absorption in this region. In cyclohexane α-tocopherol had a maximum absorption at 298 mμ ($E^{1\%}_{1\,cm.}$ 85).

Analytical values for carbon and hydrogen are given but are of little value for distinguishing between the individual esters. Some experiments with Wijs solution indicated that determinations of the iodine values for the esters by this method were not reproducible.

The author thanks Messrs. Vitamins Ltd. for financial assistance, and Professor H. Burton for his interest in this work. Dr. D. A. F. Munday kindly prepared the pure oleic acid and Mrs. M. Phillips gave some technical assistance. The work was carried out under the tenure of a grant from the Central Research Fund of the University of London.

QUEEN ELIZABETH COLLEGE, UNIVERSITY OF LONDON,
LONDON, W.8.

[*Received, April 1st*, 1959.]

628. *The Synthesis of 9-Alkyl- or 9-Aryl-9-arsafluorenes or -9-stibiafluorenes.*

By DENYS M. HEINEKEY and IAN T. MILLAR.

9-ARSA- and 9-STIBIA-FLUORENES having an alkyl or aryl substituent in the 9-position have normally been prepared by the cyclisation of arsonic, arsinic, stibonic or stibinic acids, or chloro-arsines or -stibines, followed by introduction of the alkyl or aryl substituent by reaction of the appropriate Grignard reagent with the 9-halogeno-compound.[1]

9-Methyl-9-arsafluorene has also been prepared by the thermal decomposition of certain cyclic quaternary diarsonium salts.[2] We now record the synthesis of 9-methyl-9-arsafluorene and 9-phenyl-9-stibiafluorene by the interaction of 2,2′-dilithiodiphenyl and the appropriate dihalogeno-arsine or -stibine. We find that 2,2′-dilithiodiphenyl is conveniently prepared by the action of lithium on 2,2′-dibromo- or 2,2′-di-iodo-diphenyl, but the dibromo-compound is more readily available.

By the action of other alkyl- or aryl-dihalogeno-arsines or -stibines on the dilithio-compound, a variety of 9-alkyl- and 9-aryl-9-arsafluorenes and -stibia-fluorenes should be obtainable in good yield.

Experimental.—*9-Methyl-9-arsafluorene.* 2,2′-Dibromodiphenyl (5·5 g.) in ether (100 ml.) was added slowly to lithium foil (1 g.) under nitrogen during 1 hr., so that the mixture boiled gently. After being stirred for 2·5 hr., the solution of 2,2′-dilithiodiphenyl was separated from insoluble material by decantation under nitrogen. Di-iodomethylarsine (5·5 g.) in benzene (50 ml.) was added during 20 min., and the mixture was then boiled for 30 min., cooled in ice, and hydrolysed with cold air-free water. The separated organic layer was dried (Na_2SO_4), evaporated, and distilled under nitrogen, giving diphenyl (b. p. 75°/0·01 mm., 0·1 g.) followed by the arsafluorene, b. p. 102—104°/0·01 mm. (2·25 g., 60%), which, crystallised from methanol, had m. p. 40—41° (lit.,[2] m. p. 41—41·5°). It gave a methiodide monohydrate, m. p. and mixed m. p. 206—207° (lit.,[2] m. p. 206—207°), and methopicrate, m. p. and mixed m. p. 215° (lit.,[2] m. p. 214·5—215·5°).

9-Phenyl-9-stibiafluorene. Phenyldi-iodostibine, prepared as described by Schmidt [3] and

[1] See, *e.g.*, Mann, "The Heterocyclic Derivatives of Phosphorus, Arsenic, Antimony, Bismuth and Silicon," Interscience Publ. Inc., New York, 1950; Campbell and Morrill, *J.*, 1955, 1662; Campbell and Poller, *J.*, 1956, 1195.

[2] Heaney, Heinekey, Mann, and Millar, *J.*, 1958, 3838.

[3] Schmidt, *Annalen*, 1920, **421**, 219.

XUM

recrystallised from light petroleum (b. p. 60—80°), had m. p. 62° (lit.,[3] 69°) (Found: C, 16·2; 1·4. Calc. for $C_6H_5I_2Sb$: C, 16·0; H, 1·1%). Phenyldi-iodostibine (8 g.) in benzene (50 ml.) was added during 20 min. to a solution of 2,2′-dilithiodiphenyl, prepared as described above, under nitrogen. The mixture was boiled under reflux for 1 hr., then cooled and hydrolysed as before: the solvents were removed under nitrogen from the dried organic layer. The residue was dissolved in benzene and percolated through a short column of alumina; removal of solvent from the filtrate and recrystallisation of the residue from ethanol gave the colourless *stibiafluorene* m. p. 101° (3·0 g., 50%) (Found: C, 61·0; H, 3·9. $C_{18}H_{13}Sb$ requires C, 61·6; H, 3·75%). The ultraviolet absorption spectrum of this compound in the region 230—300 mμ shows a close similarity to that of 9-*p*-tolyl-9-stibiafluorene, recorded by Campbell and Poller.[4] The 9-phenyl compound shows $\lambda_{max.}$ 287 mμ (ε 13,700) and $\lambda_{min.}$ 276 mμ (ε 11,800), whereas the 9-*p*-tolyl compound [4] shows $\lambda_{max.}$ 286 mμ (ε 12,100) and $\lambda_{min.}$ 275 mμ (ε 10,900), both in ethanol.

We are indebted to the Department of Scientific and Industrial Research for a grant (to D. M. H.).

University College of North Staffordshire,
Keele, Staffordshire. [*Received, April 8th*, 1959.]

[4] Campbell and Poller, *Chem. and Ind.*, 1953, 1126; Campbell, *J.*, 1955, 3116.

629. *Thioxan and 2,2′-Dihydroxydiethyl disulphide.*

By K. J. M. Andrews and F. N. Woodward.

Hitherto thioxan $O\langle CH_2{\cdot}CH_2 \rangle S$ has been prepared by two methods, neither of which gave high yields. Clarke prepared it by the interaction of 2,2′-di-iododiethyl ether and alcoholic potassium sulphide,[1] and it was later obtained as a by-product when 2,2′-dichlorodiethyl ether was treated with sodium hydrogen sulphide.[2] It has also been produced by heating thiodiglycol with an equal weight of potassium hydrogen sulphate for several hours at 210°, after which a mixture of water, thioxan, and dithian was obtained by distillation.[3] An improved dehydration method has now been devised by using sulphuric acid as dehydrating agent which gives a pure product in 60% yield.

2,2′-Dihydroxydiethyl disulphide is normally obtained by oxidising 2-hydroxyethane-1-thiol with hydrogen peroxide, ferric chloride, or hypobromous acid.[4,5] A method using air as oxidant has now been devised.

Experimental.—Thioxan. A mixture of thiodiglycol (100 g.) and concentrated sulphuric acid (5 g.) was heated at 160° and the distillate was collected. After 5 hr. a vacuum of 300—400 mm. was applied and the distillation was continued until dithian began to block the condenser. The oily layer in the distillate was separated and fractionally distilled, to give thioxan (51 g.), b. p. 148—149°/760 mm. (lit.,[6] b. p. 147°) (Found: S, 30·2. Calc. for C_4H_8OS: S, 30·8%).

2,2′-Dihydroxydiethyl disulphide. Distilled 2-hydroxyethane-1-thiol to which was added 1% w/w of manganous sulphate and an equivalent quantity of 50% sodium hydroxide solution was stirred and heated at 55—60° under reflux. Air, washed with sodium hydroxide solution and dried (CO_2–EtOH cold trap), was drawn through at a rate of 2 l./hr. The contents of thiol found[7] after 0, 3, and 6 hr. were 95·4, 44·1, and 35·4% respectively. After removal of the unchanged thiol by distillation at 110 mm., a yield of 54% of almost pure disulphide remained. This almost all distilled at 92°/0·002 mm. (lit.,[5] b. p. 158—163°/3·5 mm.) and was characterised by preparation of the bis-α-naphthylurethane, m. p. 152° (undepressed on admixture with an authentic specimen[5]).

An air input of 10 l./hr. did not increase the rate of oxidation.

This work was carried out in a Ministry of Supply research establishment.

Roche Products, Ltd., Broadwater Road, Welwyn Garden City, Herts.
Arthur D. Little Research Institute,
Inveresk, Midlothian. [*Received, April 14th*, 1959.]

[1] Clarke, *J.*, 1912, 1806.
[2] Meadow and Reid, *J. Amer. Chem. Soc.*, 1934, **56**, 2177.
[3] Fromm and Ungar, *Ber.*, 1923, **56**, 2288.
[4] Bennett, *J.*, 1921, 418.
[5] Williams and Woodward, *J.*, 1948, 38.
[6] Johnson, *J.*, 1933, 1530.
[7] Woodward, *Analyst*, 1949, **74**, 179.

XUM

XUM

THE CHEMICAL SOCIETY

PATRON

HER MAJESTY THE QUEEN

President

H. J. Emeléus, C.B.E., M.A., D.Sc., F.R.S.

Vice-Presidents

who have filled the office of President

Sir Cyril Hinshelwood, M.A., Sc.D., F.R.S.
Sir Christopher Ingold, D.Sc., F.R.I.C., F.R.S.
E. L. Hirst, C.B.E., D.Sc., LL.D., F.R.S.
Sir Eric Rideal, M.B.E., M.A., D.Sc., F.R.S.
Sir Robert Robinson, O.M., D.Sc., LL.D., F.R.S.

Vice-Presidents

Wilson Baker, M.A., D.Sc., F.R.S.
R. D. Haworth, D.Sc., Ph.D., F.R.S.
R. P. Bell, M.A., F.R.S.
F. G. Mann, Sc.D., F.R.I.C., F.R.S.
F. Bergel, D.Sc., F.R.I.C., F.R.S.
L. E. Sutton, M.A., D.Phil., F.R.S.

Honorary Treasurer

M. W. Perrin, C.B.E., M.A., F.R.I.C.

Honorary Secretaries

J. Chatt, M.A., Sc.D., F.R.I.C.
M. J. S. Dewar, M.A., D.Phil.
A. W. Johnson, Sc.D., Ph.D., A.R.C.S.

Ordinary Members of Council

C. B. Amphlett, Ph.D., D.Sc.
A. H. Lamberton, Ph.D.
R. G. R. Bacon, Ph.D., A.R.C.S.
L. H. Long, Ph.D., A.R.C.S., D.I.C.
A. J. Birch, M.Sc., D.Phil., F.R.S.
J. D. Loudon, Ph.D., D.Sc.
G. E. Coates, M.A., D.Sc., F.R.I.C.
R. S. Nyholm, D.Sc., F.R.I.C., F.R.S.
R. C. Cookson, M.A., Ph.D.
H. T. Openshaw, M.A., D.Phil.
A. C. Farthing, M.A., B.Sc., A.R.I.C.
R. E. Richards, M.A., D.Phil., F.R.S.
I. J. Faulkner, Ph.D., F.R.I.C.
J. C. Tatlow, Ph.D., D.Sc., F.R.I.C.
R. H. Hall, Ph.D., A.R.C.S., F.R.I.C.
R. H. Thomson, D.Sc., Ph.D., F.R.I.C.
C. H. Hassall, M.Sc., Ph.D., F.R.I.C.
A. I. Vogel, D.Sc., D.I.C., F.R.I.C.
B. A. Hems, D.Sc., F.R.I.C.
W. A. Waters, Sc.D., F.R.I.C., F.R.S.
W. B. Whalley, D.Sc., Ph.D., F.R.I.C.

Ex Officio

J. W. Cook, D.Sc., F.R.I.C., F.R.S. (Chairman of the Chemical Council)
E. D. Hughes, D.Sc., F.R.I.C., F.R.S. (Chairman of the Joint Library Committee)

General Secretary

J. R. Ruck Keene, M.B.E., T.D., M.A.

Librarian

R. G. Griffin, F.L.A.

Deputy Librarian

J. Bird

XUM

INTERNATIONAL CONFERENCE ON CO-ORDINATION CHEMISTRY LONDON 1959

This Report, published as No. 13 in The Chemical Society's series of Special Publications, contains the full text of the General Lectures delivered at the Conference by the following: E. O. Fischer (Munich), H. M. N. H. Irving (Oxford), R. Nast (Heidelberg), L. E. Orgel (Cambridge), H. W. Sternberg (Pittsburgh), H. Taube (Chicago), K. Ziegler (Mülheim). The publication also includes Abstracts of the contributed papers.

Price: £2. 2s. 0d. (U.S.A. $6)

THE CHEMICAL SOCIETY
BURLINGTON HOUSE, LONDON, W.1

Printed in Great Britain by Richard Clay and Company, Ltd., Bungay, Suffolk.

XUM

XUM